



# Revolutionizing Small Cell Lung Cancer Treatment: Coordinated and Team-Based Implementation of T-Cell Engager Therapy

GO2 for Lung Cancer

Guest Presenters: Dana-Farber Cancer Institute



EXCELLENCE IN  
HEALTHCARE DELIVERY



# Welcome and Introductions

- **G02 for Lung Cancer**

- Moderator: Joelle Fathi, DNP, ARNP. Chief Healthcare Delivery Officer
- Andrew Ciupek, PhD, Associate Director, Clinical Research
- Holly Sands, M.Ed, Senior Instructional Designer

- **Dana-Farber Cancer Institute**

- Jacob Sands, MD, Thoracic Medical Oncologist, Associate Chair of the Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute
- Stephanie McDonald, MSN, FNP-BC, AOCNP, Nurse Practitioner, Thoracic Oncology Program
- Eileen, Small Cell Lung Cancer Patient
- Leila Rostamnjad, PHARMD, BCOP: Thoracic Clinical Pharmacy Specialist
- Kara Stocks, PA-C: Medical Oncology – Inpatient Implementation
- Michelle Dupille, RN, BSN, OCN: Thoracic Oncology Nurse Navigator



EXCELLENCE IN  
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# Revolutionizing Small Cell Lung Cancer Treatment: Coordinated and Team-Based Implementation of T-Cell Engager Therapy



# Behind Every Breakthrough Treatment – Eileen's Story

- Eileen's journey
- Eileen shares her personal experience from diagnosis to starting T-Cell Engager Therapy
- Insights into her current symptoms and treatment response

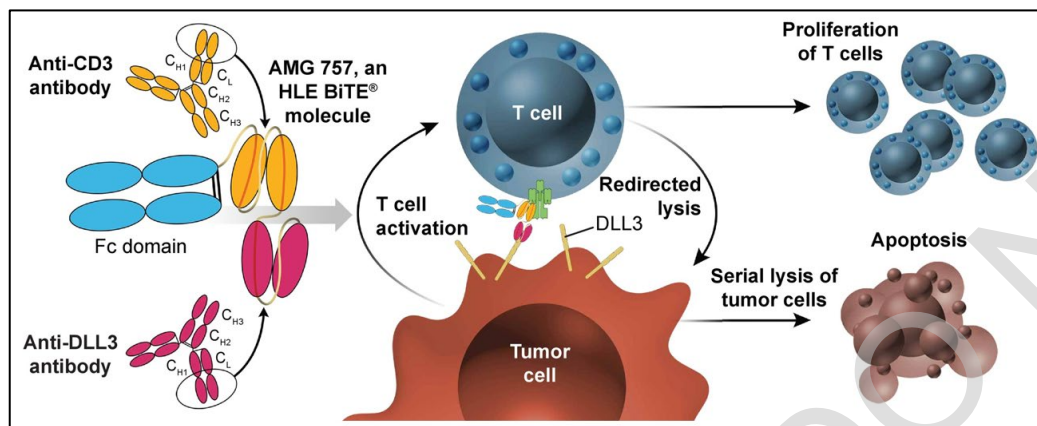
# Treatment Efficacy: Overview of T-Cell Engager Therapy

**Presenter:** Jacob Sands

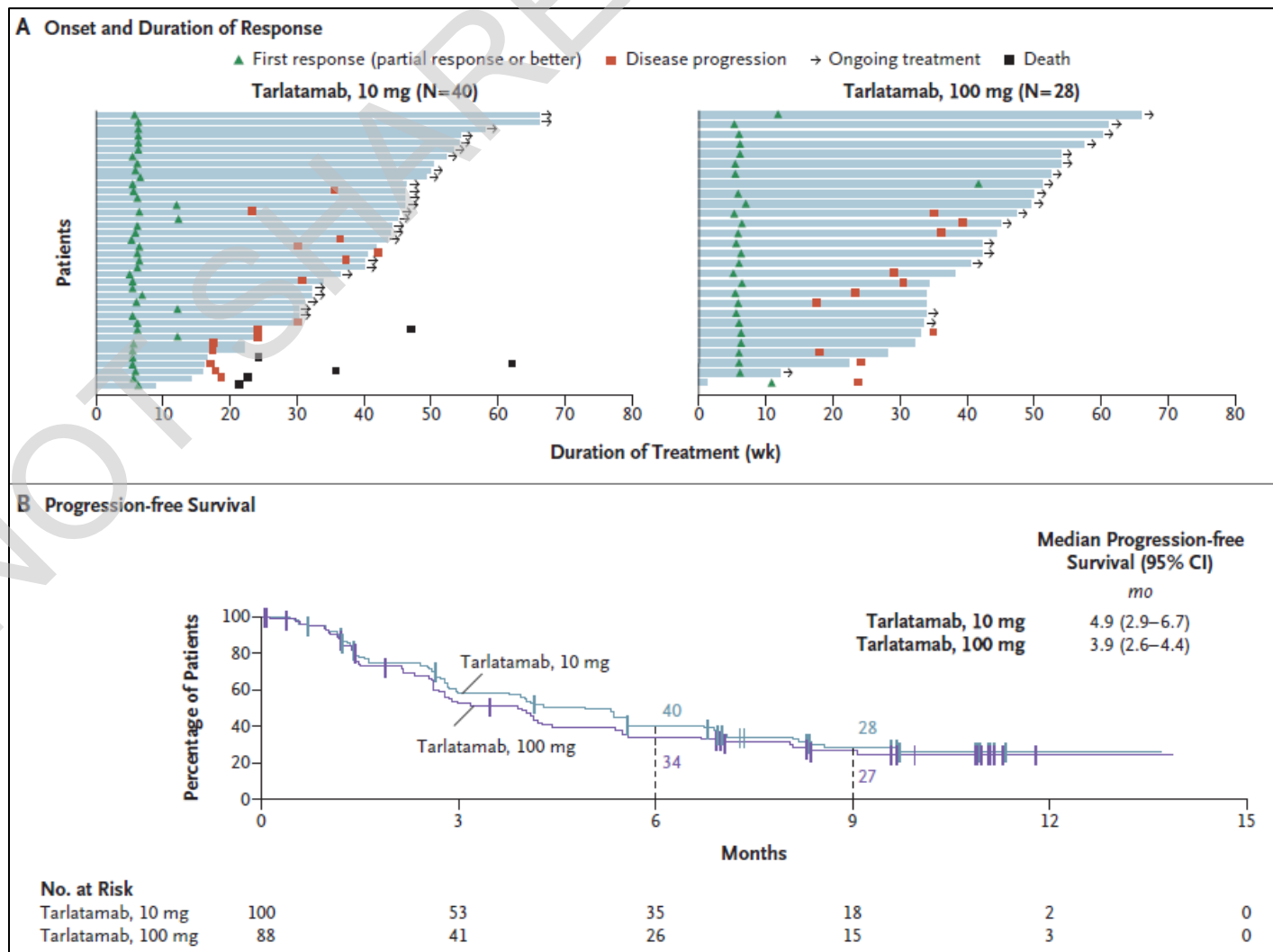
- Overview of T-Cell Engager Therapy
- Mechanism of action
- Current clinical indications
- Recent advancements and research findings

# Tarlatamab

- Bi-specific T-cell engager binds tumor cells (DLL-3) and T-cells (CD3)



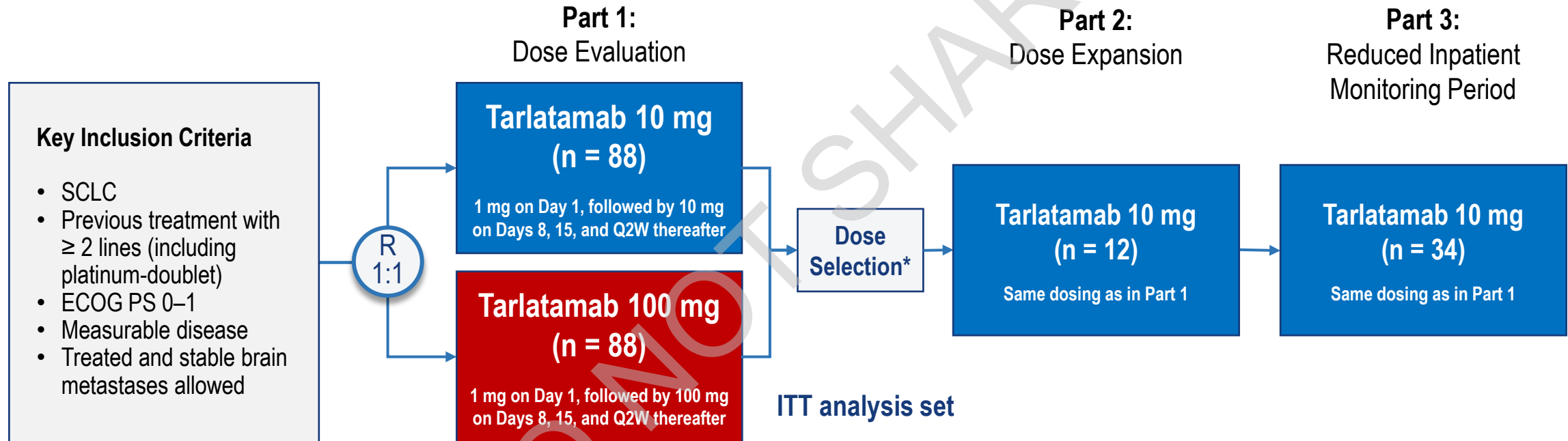
Marie-Anne Damiette Smit, et al. ASCO Poster 2019



Ahn MJ et al. *N Engl J Med*. 2023;Oct 20.

# DeLLphi-301 Study Design

- Phase 2, open-label study (NCT05060016)



**Primary Endpoint:** ORR per RECIST 1.1 by BICR

**Secondary Endpoints Included:** DOR, DCR, PFS per RECIST 1.1 by BICR, OS, TEAEs, tarlatamab serum concentrations

Data cutoff was January 12, 2024 for all efficacy and safety outcomes, except for OS. For OS, the data cutoff was May 16, 2024 to obtain mature OS data with a median follow-up of 20.7 months.

\*Once 30 patients per dose level had the opportunity to confirm an objective response after the first post-treatment scan or  $\geq 13$  weeks of follow-up, whichever occurred first.

**BICR**, blinded independent central review; **DCR**, disease control rate; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ITT**, intention-to-treat; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression-free survival; **Q2W**, every 2 weeks; **R**, randomization; **RECIST**, Response Evaluation Criteria in Solid Tumors; **SCLC**, small cell lung cancer; **TEAE**, treatment-emergent adverse event.

# Baseline Characteristics

|                                                                            | Parts 1 + 2<br>Tarlatamab 10 mg<br>(n = 100) | Part 3<br>Tarlatamab 10 mg<br>(n = 34) |
|----------------------------------------------------------------------------|----------------------------------------------|----------------------------------------|
| Median age, years (range)                                                  | 64 (35–82)                                   | 66 (49–80)                             |
| Male, %                                                                    | 72                                           | 71                                     |
| Asian/Black or African American/White,* %                                  | 41 / 0 / 58                                  | 6 / 3 / 91                             |
| Patients who ever smoked/patients who never smoked, %                      | 92 / 8                                       | 97 / 3                                 |
| ECOG performance status: 0/1, %                                            | 26 / 74                                      | 29 / 71                                |
| Prior lines of therapy, median (range)                                     | 2 (1–6) <sup>†</sup>                         | 2 (2–6)                                |
| 2 prior lines of therapy, %                                                | 65                                           | 65                                     |
| ≥ 3 prior lines of therapy, %                                              | 33                                           | 35                                     |
| Prior anti-PD-(L)1 treatment, %                                            | 74                                           | 82                                     |
| < 90 days to progression after first-line platinum therapy, <sup>‡</sup> % | 28                                           | 21                                     |
| Brain/liver metastases, %                                                  | 23 / 39                                      | 12 / 35                                |
| DLL3 expression (> 0%), n/N evaluable (%)                                  | 80 / 83 (96)                                 | 15 / 16 (94)                           |

Data cutoff, January 12, 2024. Median follow-up was 16.6 months. \*No patients of American Indian, Alaska Native, Native Hawaiian, or other Pacific Islander race were enrolled. <sup>†</sup>Two patients were treated with one prior line of therapy. <sup>‡</sup>Platinum sensitivity was calculated as end of first-line platinum therapy to date of first progression. **DLL3**, delta-like ligand 3; **ECOG**, Eastern Cooperative Oncology Group; **PD-(L)1**, programmed cell death (ligand) 1 protein.

# Tarlatamab Anti-Cancer Activity

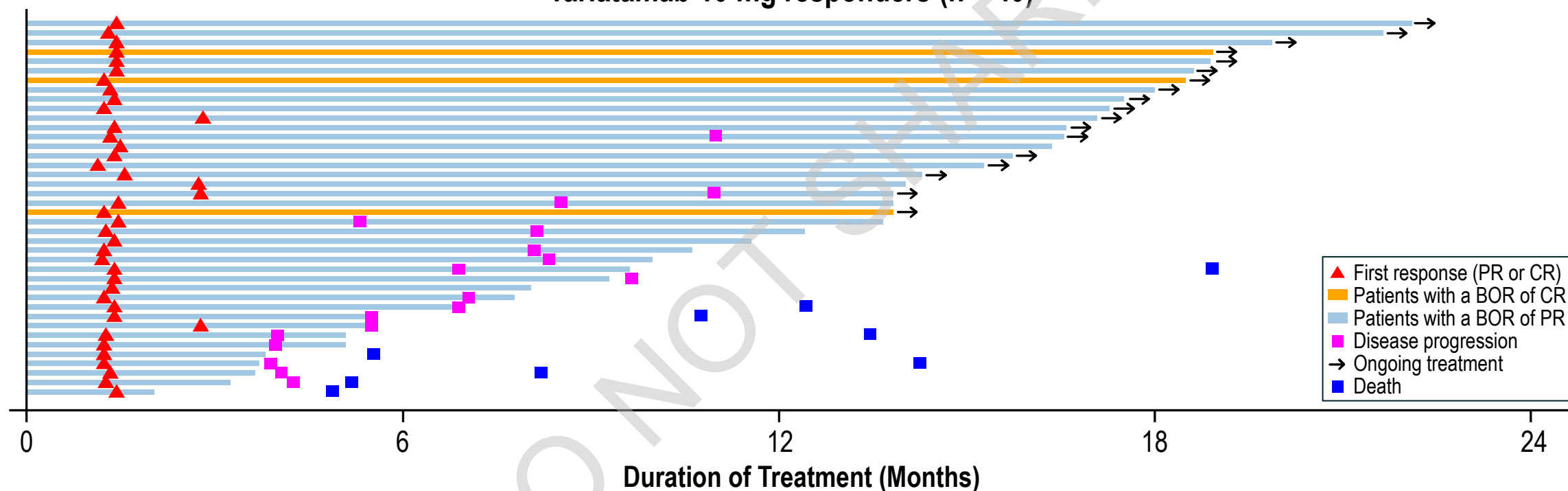
| Outcome                                                 | Part 1 + 2<br>Tarlatamab 10 mg<br>(N = 100) |
|---------------------------------------------------------|---------------------------------------------|
| <b>Objective response rate, n (%)</b><br>(95% CI for %) | 40 (40)<br>(30.3–50.3)                      |
| Complete response                                       | 3 (3)                                       |
| Partial response                                        | 37 (37)                                     |
| Stable disease                                          | 30 (30)                                     |
| Progressive disease                                     | 20 (20)                                     |
| Not evaluable / no post-baseline scan*                  | 10 (10)                                     |
| <b>Disease control rate, n (%)</b><br>(95% CI for %)    | 70 (70)<br>(60.0–78.8)                      |

**Tarlatamab 10 mg demonstrated anti-cancer activity in heavily pretreated SCLC, with an ORR of 40%**

Data cutoff, January 12, 2024. Median follow-up was 16.6 months. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. \*Patients who were not evaluable or did not have post-baseline scans were considered non-responders for the response analysis.  
 CI, confidence interval; ITT, intention-to-treat; **ORR**, objective response rate; **SCLC**, small cell lung cancer.

# Duration of Response and Time on Treatment

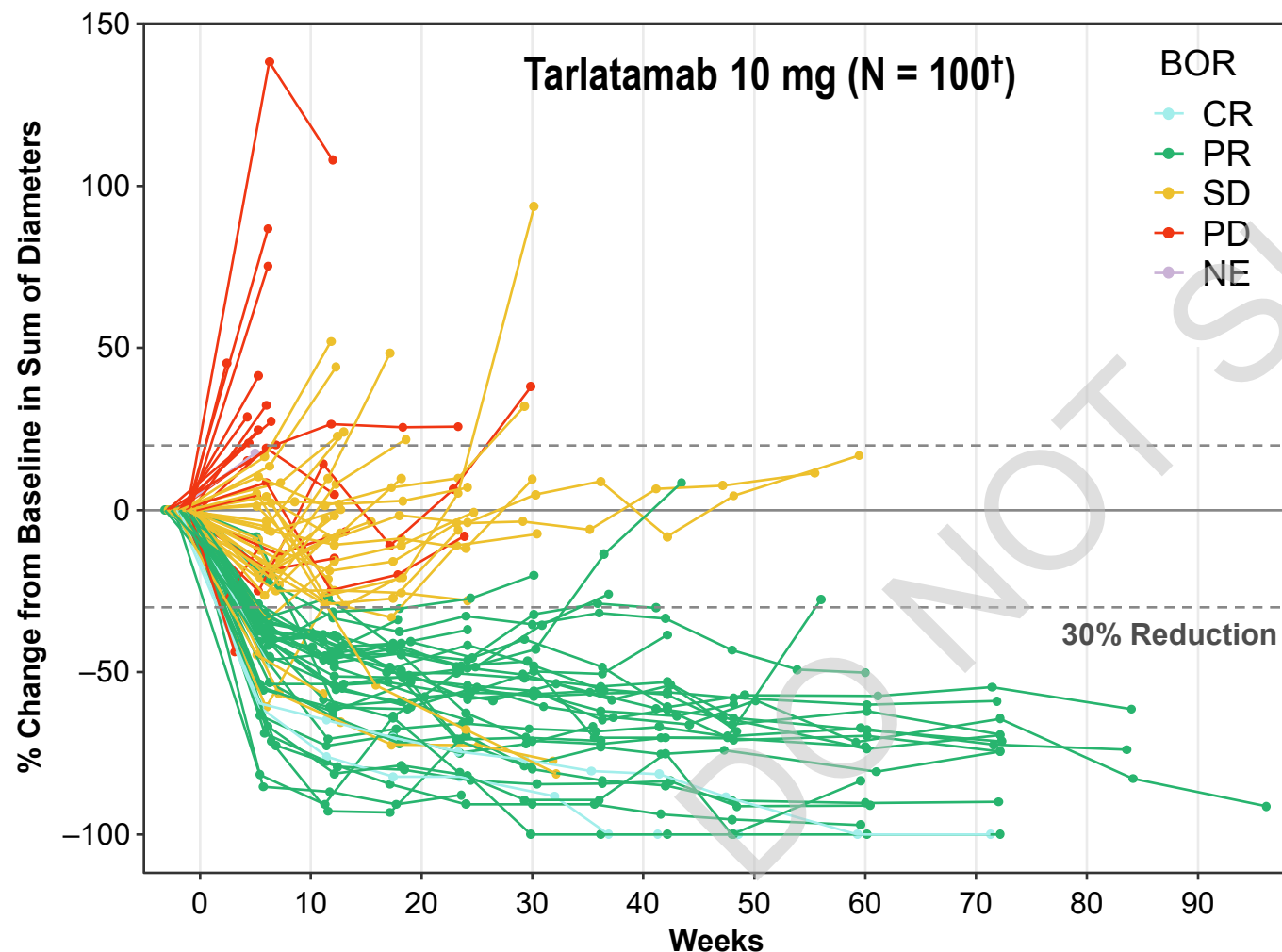
Tarlatamab 10 mg responders (n = 40)



- Median time to response was 1.4 months (IQR, 1.3–1.4)
- Median DOR was 9.7 months (95% CI, 6.9–NE) with 17/40 (43%) of responses ongoing at data cutoff

Data cutoff was January 12, 2024. Median follow up for DOR was 15.1 months. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety sub-study and was not included in this response analysis. BOR, best overall response; CR, complete response; DOR, duration of response; ITT, intention-to-treat; IQR, interquartile range; NE, not estimable; PR, partial response.

# Sustained Disease Control\*



- Tumor shrinkage was seen in 72% of patients
- The median duration of disease control was 6.9 months (95% CI, 5.4–8.6)

**26 patients (26%; 3 CR, 20 PR, 3 SD) had sustained disease control\* ≥ 52 weeks**

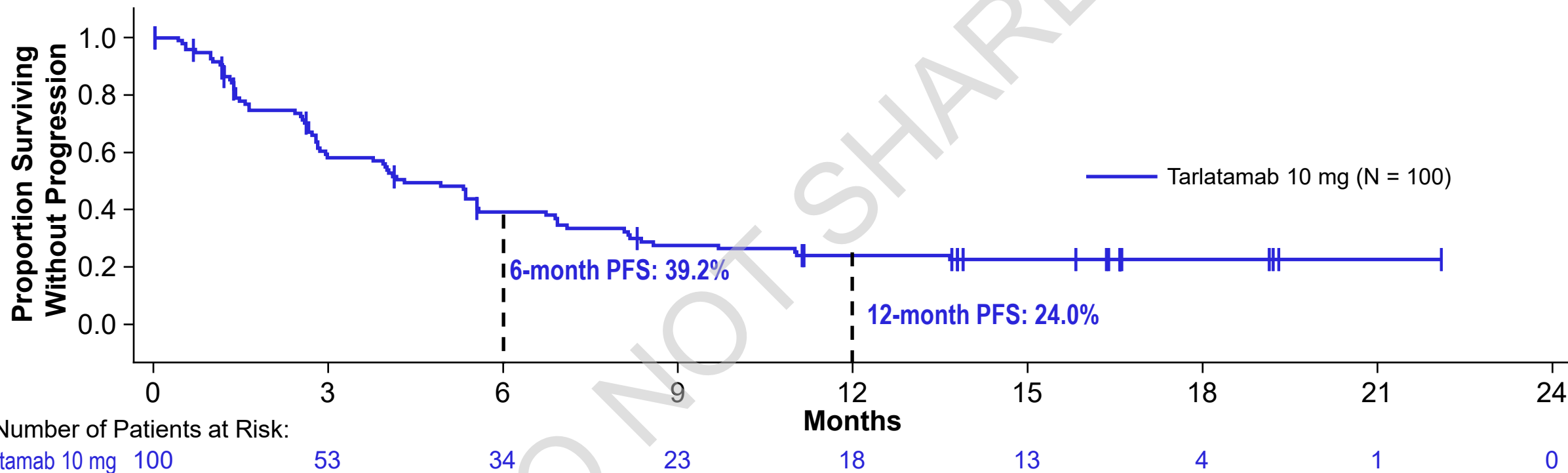
Data cutoff, January 12, 2024. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety substudy and was not included in this response analysis.

\*Sustained disease control was defined as disease control (CR, PR, or SD) with time on treatment ≥ 52 weeks.

<sup>†</sup>Seven patients did not have a postbaseline scan.

**BOR**, best overall response; **CR**, complete response; **ITT**, intention-to-treat; **NE**, not evaluable; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease.

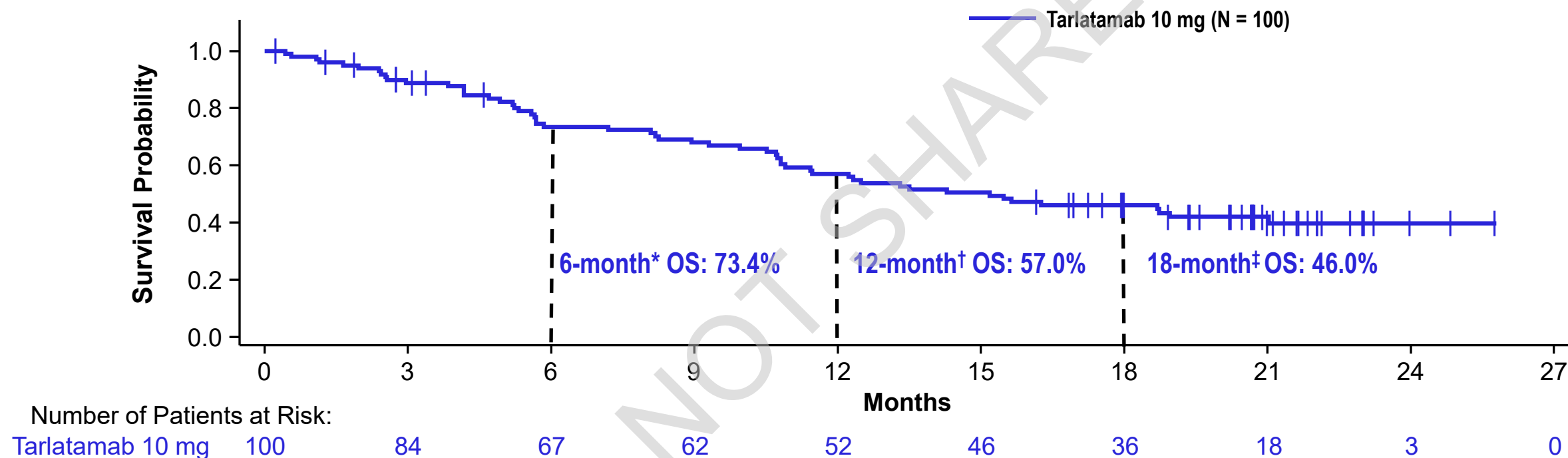
# Progression-Free Survival



- Median PFS was 4.3 months (95% CI, 2.9–5.6)

Data cutoff, January 12, 2024. Median follow-up for PFS was 16.4 months. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in the ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. ITT, intention-to-treat; PFS, progression-free survival.

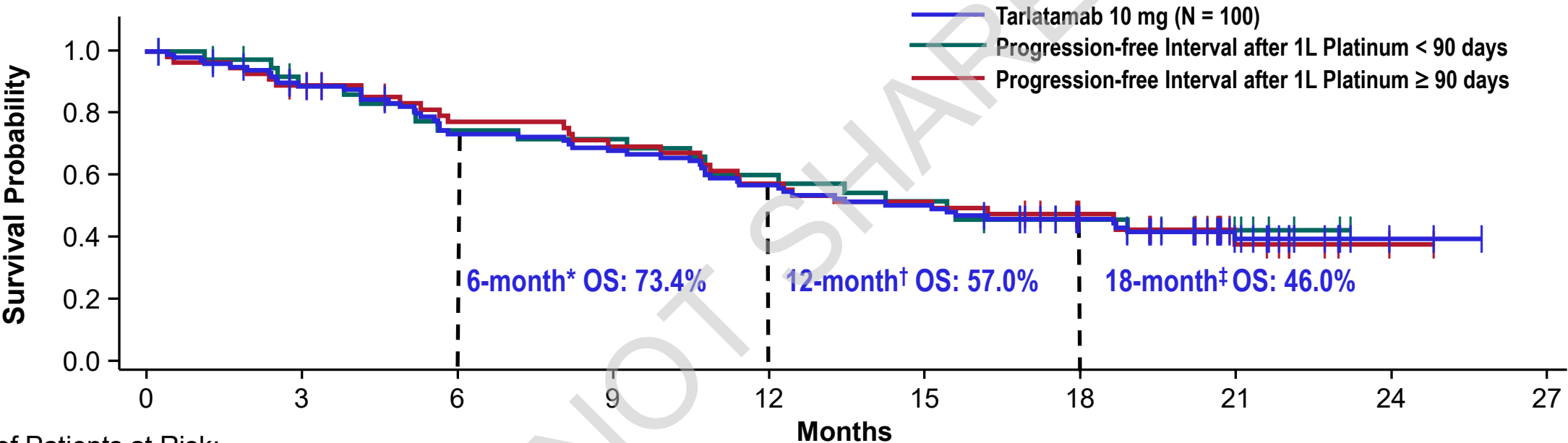
# Overall Survival



**Median OS was 15.2 months (95% CI, 10.8–NE)**

Median follow-up for OS was 20.7 months. Data cutoff, May 16, 2024. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. \*95% CI, 63.2–81.2. †95% CI, 46.3–66.3. ‡95% CI, 35.6–55.8. Progression-free interval after first line platinum treatment is defined as days from the last first line platinum treatment to disease progression or start of second line treatment, whichever is earlier. ITT, intention-to-treat; NE, not estimable; OS, overall survival.

# Overall Survival



Number of Patients at Risk:

|                  |     |    |    |    |    |    |    |    |   |   |
|------------------|-----|----|----|----|----|----|----|----|---|---|
| Tarlatamab 10 mg | 100 | 84 | 67 | 62 | 52 | 46 | 36 | 18 | 3 | 0 |
| < 90 days        | 39  | 31 | 26 | 25 | 21 | 18 | 13 | 7  | 0 |   |
| ≥ 90 days        | 55  | 48 | 39 | 35 | 29 | 26 | 21 | 9  | 2 | 0 |

**OS was similar regardless of progression-free interval after 1L platinum treatment (< 90 d vs ≥ 90 d)**

Median follow-up for OS was 20.7 months. Data cutoff, May 16, 2024. The efficacy analysis set consists of patients in Parts 1 and 2 (N = 100). One patient did not receive tarlatamab 10 mg but was included in ITT analysis. Part 3 was a safety substudy and was not included in this response analysis. \*95% CI, 63.2–81.2. †95% CI, 46.3–66.3. ‡95% CI, 35.6–55.8. Progression-free interval after first line platinum treatment is defined as days from the last first line platinum treatment to disease progression or start of second line treatment, whichever is earlier. ITT, intention-to-treat; NE, not estimable; OS, overall survival.

# DeLLphi-301 Conclusions

- With extended follow-up, tarlatamab 10 mg Q2W demonstrated durable response and impressive survival outcomes
  - Median DOR was 9.7 months
  - Median OS was 15.2 months with a Kaplan-Meier estimate for OS at 18 months of 46%
- Tarlatamab demonstrated long-term tolerability with no new safety concerns
- The phase 3 DeLLphi-304 study (NCT05740566) comparing the efficacy and safety of tarlatamab (10 mg Q2W) with standard-of-care chemotherapy is currently in progress<sup>4</sup>

**Tarlatamab demonstrated durable response and unprecedented survival outcomes with long-term tolerability in patients with previously treated SCLC**

DOR, duration of response; OS, overall survival; Q2W, every 2 weeks; SCLC, small cell lung cancer.

# Managing Side Effects and Safety Considerations

**Presenter:** Stephanie McDonald, NP Thoracic Oncology

- Common side effects of T-Cell Engager Therapy
- Safety considerations and monitoring strategies
- Planning for side effect management
- Patient education and support initiatives

# Common and Adverse Events

| DeLLphi-301    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|----------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Adverse Events | Observations                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Patient Management                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| CRS            | <ul style="list-style-type: none"> <li>CRS incidence = 53%                             <ul style="list-style-type: none"> <li>Grade 1 (fever) in 32%</li> <li>Grade 2 (hypoxia and hypotension) in 20%</li> <li>Grade 3 in &lt; 1%</li> </ul> </li> <li>Primarily occurred following first or second dose</li> <li>Median time to onset: 13.7 hours (IQR, 9.3 – 33.2)</li> </ul>                                                                                                                                                                    | <ul style="list-style-type: none"> <li>Sites monitored patients closely following first two doses</li> <li>CRS was generally managed with supportive care including antipyretics (acetaminophen), IV hydration, and/or glucocorticoids</li> <li>Sites were required to have corticosteroids and tocilizumab available onsite (or situximab if tocilizumab was not available)</li> </ul>                                                                                                        |
| ICANS          | <ul style="list-style-type: none"> <li>ICANS incidence = 10%</li> <li>Events were Grade 1 or 2</li> <li>Median time to onset: 30 days (IQR, 13 – 47)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>ICANS symptoms included confusion, impaired attention, motor weakness/ findings, dysgraphia, and increased tone</li> <li>Grade 1 ICANS was managed with supportive care</li> <li>Grade 2 was managed with steroid (eg, dexamethasone)</li> </ul>                                                                                                                                                                                                        |
| Dysgeusia      | <ul style="list-style-type: none"> <li>Dysgeusia incidence = 32%</li> <li>Median time to onset: 34 days (IQR, 21–51)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>Investigators used previously published strategies for managing dysgeusia including:                             <ul style="list-style-type: none"> <li>Nutritional counseling by registered dietitian</li> <li>Maintenance of good oral dental hygiene</li> <li>Maintenance of adequate hydration (~ 1.5 – 2 L of water/day)</li> <li>Periodic chewing of cardamom; inhaling smell of cloves and lemon ≥ 2x/day for ~15 seconds</li> </ul> </li> </ul> |
| Neutropenia    | <ul style="list-style-type: none"> <li>Neutropenia incidence = 16%</li> <li>Median time to onset: 56 days (IQR, 30 – 86)</li> <li>Febrile neutropenia in &lt; 1%</li> <li>Did not result in treatment discontinuation</li> </ul>                                                                                                                                                                                                                                                                                                                    | <ul style="list-style-type: none"> <li>Institution-specific protocols were suggested for management of grade 1-2 neutropenia</li> <li>For grade ≥ 3 neutropenia:                             <ul style="list-style-type: none"> <li>Use of granulocyte colony-stimulating factor (G-CSF) was permitted</li> <li>Treatment interruption were considered until severity decreases to grade 2 or lower</li> </ul> </li> </ul>                                                                     |
| Elevated LFTs  | <ul style="list-style-type: none"> <li>ALT increase incidence = 11%                             <ul style="list-style-type: none"> <li>Grade 3 in 1.5%</li> <li>Median time to onset: 29 days (IQR, 7 – 113)</li> </ul> </li> <li>AST increase incidence = 11%                             <ul style="list-style-type: none"> <li>Median time to onset: 51 days (IQR, 3 – 196)</li> </ul> </li> <li>Generally transient with no evidence suggesting extensive hepatocellular damage</li> <li>Did not result in treatment discontinuation</li> </ul> | <ul style="list-style-type: none"> <li>Investigators documented baseline levels of liver enzymes and bilirubin prior to start of tarlatamab</li> <li>LFTs were monitored with each tarlatamab dose and as clinically indicated</li> </ul>                                                                                                                                                                                                                                                      |

# Dosing and Administration

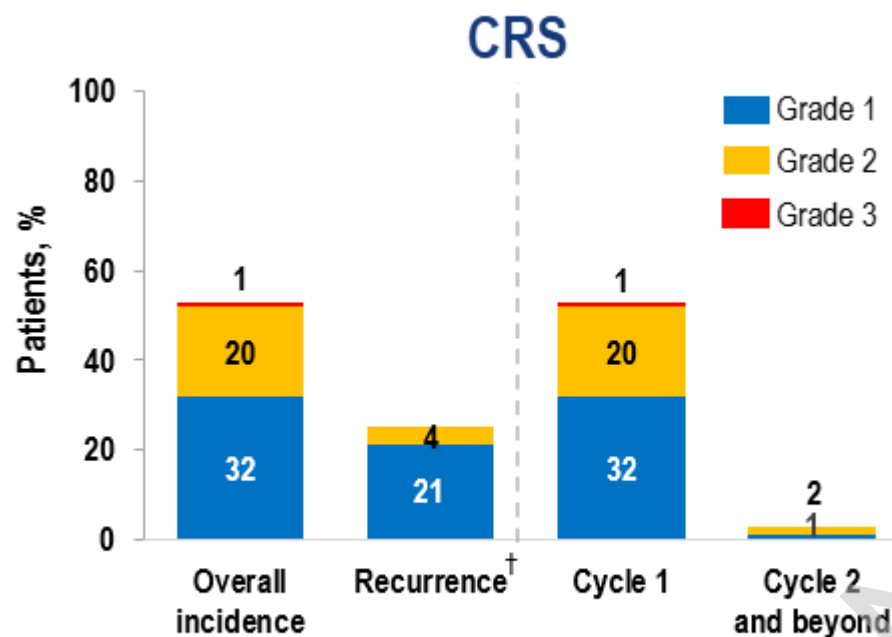
| Drug       | Dose | Dose Units | Route | Schedule                | Cycle Length |
|------------|------|------------|-------|-------------------------|--------------|
| Tarlatamab | 1    | mg         | IV    | C1D1                    | 28 days      |
|            | 10   | mg         | IV    | C1D8 , C1D15            | 28 days      |
|            | 10   | mg         | IV    | C2D1 , C2D15 and beyond | 28 days      |

| Drug       | Dose | Dose Units | Schedule              | Monitoring                               |
|------------|------|------------|-----------------------|------------------------------------------|
| Tarlatamab | 1    | mg         | C1D1                  | 22-24 hours (BWH) from start of infusion |
|            | 10   | mg         | C1D8                  |                                          |
|            | 10   | mg         | C1D15*                | 6-8 hours post infusion                  |
|            | 10   | mg         | C2D1 , C2D15*         |                                          |
|            | 10   | mg         | C3 D1, C3D15*         | 3-4 hours post infusion                  |
|            | 10   | mg         | C4D1,C4D15*           |                                          |
|            | 10   | mg         | C5D1,C5D15 and beyond | 2 hours post infusion                    |

\*Extended monitoring if patient experiences Grade  $\geq 2$  CRS, ICANS or neurological toxicity during prior treatments

- Reginal campus Administration: C3 and beyond

# CRS Incidence and Timing



| CRS severity, % (n/N)                                                         | Grade 1               | Grade 2        | Grade 3      | Grade 4 | Grade 5 |
|-------------------------------------------------------------------------------|-----------------------|----------------|--------------|---------|---------|
| N = number of patients experiencing CRS                                       | 60%<br>(42/70)        | 39%<br>(27/70) | 1%<br>(1/70) | 0       | 0       |
| Timing of CRS events                                                          |                       |                |              |         |         |
| Median (IQR) time to onset of first CRS event from the first tarlatamab dose  | 13.7 hours (9.3–33.2) |                |              |         |         |
| Median (IQR) time to onset of first CRS event from last prior tarlatamab dose | 15.4 hours (9.5–28.1) |                |              |         |         |
| Median (IQR) time to onset of grade ≥2 CRS from last prior tarlatamab dose    | 15.4 hours (9.6–27.9) |                |              |         |         |
| Median (IQR) duration of CRS                                                  | 3 days (2–5)          |                |              |         |         |

- CRS primarily occurred after the first or second dose in cycle 1, with most events of grade 1 or 2

\*ICANS includes associated neurologic events based on a broad search using 61 selected preferred terms from MedDRA version 26.0. <sup>†</sup>A CRS event is considered a recurrent event if it occurred at a subsequent dose after the first CRS event during cycle 1.

<sup>‡</sup>Based on Kaplan-Meier estimates. TEAE data are reported. <sup>§</sup>Based on 22 events. CI, confidence interval; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; MedDRA, Medical Dictionary for Regulatory Activities.

# CRS Grading and Management

| CRS Grade | Defining Symptoms                                                                                                                                                                                                                                                                                       | Management <sup>a</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grade 1   | Fever $\geq 38^{\circ}\text{C}$ , without hypotension or hypoxia                                                                                                                                                                                                                                        | <ul style="list-style-type: none"> <li>Symptomatic treatment (e.g., paracetamol/acetaminophen) for fever</li> <li>Culture, if neutropenic cover w/ abx</li> </ul>                                                                                                                                                                                                                                                                                                                                                                 |
| Grade 2   | <ul style="list-style-type: none"> <li>Fever <math>\geq 38^{\circ}\text{C}</math>,</li> <li>Hypotension not requiring vasopressors, and/or</li> <li>Hypoxia requiring low-flow nasal cannula</li> </ul>                                                                                                 | <ul style="list-style-type: none"> <li>Supplemental oxygen when oxygen saturation <math>&lt; 90\%</math> on room air</li> <li>Intravenous fluids when SBP <math>&lt; 85</math> mmHg and/or persistent tachycardia (heart rate <math>&gt; 120</math> bpm) or symptomatic (eg dizziness/lightheadedness)</li> <li>If not responding to fluids, page oncologist and given Dex 8-10 mg</li> <li>If not responding to dex (give about an hour) then consider Tocilizumab (dose is 8mg/kg). Expect to take 1 hour to kick in</li> </ul> |
| Grade 3   | Severe symptoms defined as temperature $\geq 38^{\circ}\text{C}$ with: <ul style="list-style-type: none"> <li>HD instability requiring a vasopressor) or</li> <li>Worsening hypoxia or respiratory distress requiring high-flow nasal canula (<math>&gt; 6</math> L/min oxygen) or face mask</li> </ul> | <ul style="list-style-type: none"> <li>Supplemental oxygen</li> <li>Vasopressor <math>\pm</math> vasopressin</li> <li>IV Dexamethasone (or equivalent), and/or</li> <li>Tocilizumab, can consider additional dose but would need to discuss further</li> </ul>                                                                                                                                                                                                                                                                    |
| Grade 4   | Fever (Temp $\geq 38^{\circ}\text{C}$ ) WITH Hypotension (requiring multiple vasopressors, excluding vasopressin) And/Or Hypoxia (requiring positive pressure, not attributable to another cause)                                                                                                       | <ul style="list-style-type: none"> <li>Intensive monitoring, e.g., ICU care</li> <li>See Grade I, II and III for supportive care</li> <li>Tocilizumab 8 mg/kg IV may be administered per provider discretion</li> </ul>                                                                                                                                                                                                                                                                                                           |

Lee DW et al. *Biol Blood Marrow Transplant.* 2019;25(4):625-638.

## Practical Management of Adverse Events in Patients Receiving Tarlatamab, a DLL3-targeted Bispecific T-cell Engager Immunotherapy, for Previously Treated Small Cell Lung Cancer

**Running Title:** Tarlatamab adverse event management

Jacob M. Sands MD<sup>1†</sup>, Stéphane Champiat MD, PhD<sup>2\*†</sup>, Horst-Dieter Hummel MD<sup>3</sup>, Kelly G. Paulson MD, PhD<sup>4</sup>, Hossein Borghaei DO<sup>5</sup>, Jean Bustamante Alvarez MD<sup>6</sup>, David P. Carbone MD, PhD<sup>7</sup>, Jennifer W. Carlisle MD<sup>8</sup>, Noura J. Choudhury MD<sup>9†</sup>, Jeffrey M. Clarke MD<sup>10</sup>, Shirish M. Gadgeel MD<sup>11</sup>, Hiroki Izumi MD, PhD<sup>12</sup>, Alejandro Navarro MD<sup>13</sup>, Sally C. M. Lau MD<sup>14</sup>, Philip E. Lammers MD<sup>15</sup>, Shuang Huang PhD<sup>16</sup>, Ali Hamidi MD<sup>16</sup>, Sujoy Mukherjee MD<sup>16</sup>, Taofeek K. Owonikoko MD, PhD<sup>17</sup>

# Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS)

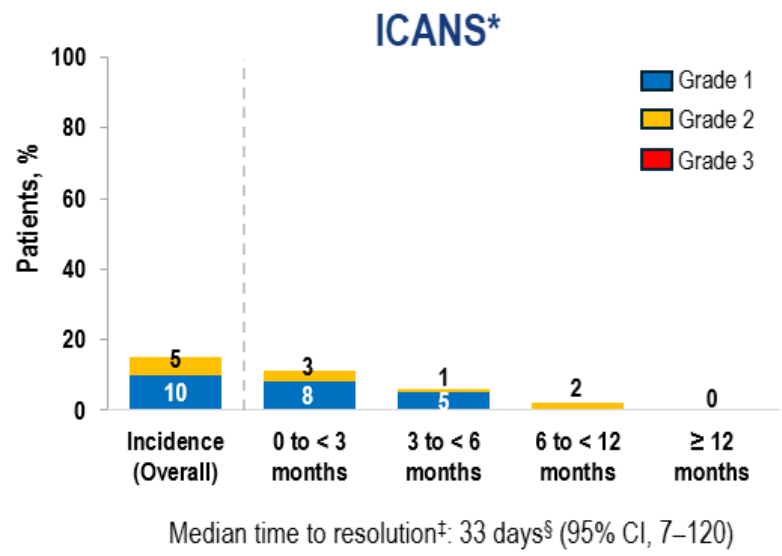
## Signs and symptoms

- **Trouble speaking, memory loss, or personality changes**
- **confusion, feeling disoriented, slow thinking, or not being able to think clearly**
- **Weakness or numbness of the arms or legs**
- Problems with walking, or loss of balance or coordination
- Shaking (tremors)
- Headache
- Numbness or tingling of the hands or feet
- Trouble sleeping
- Fainting or loss of consciousness
- Feeling like you have no energy
- Seizure

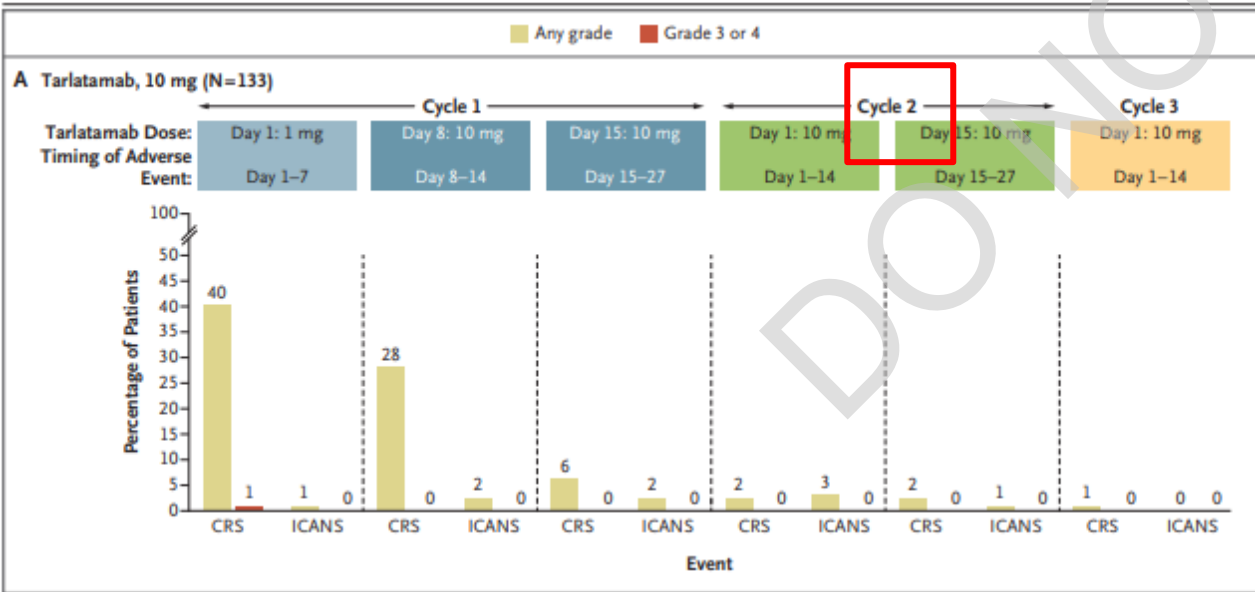
Ahn MJ et al. *N Engl J Med*. 2023;389(22):2063-2075.

# Tarlatamab: ICANS Onset and Duration

ICANS\* occurred infrequently, primarily with early onset (< 6 months) and all events of grade 1 or 2



| Severity of ICANS and associated neurological events, % (n/N)                                                                                                                                                                                                             | Grade 1                    | Grade 2       | Grade 3 | Grade 4 | Grade 5 |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|---------------|---------|---------|---------|
| N = number of patients experiencing ICANS and associated neurological events                                                                                                                                                                                              | 54%<br>(7/13)              | 46%<br>(6/13) | 0       | 0       | 0       |
| Median (IQR) time to onset of first ICANS event from the first tarlatamab dose                                                                                                                                                                                            | 30 days (13–47)            |               |         |         |         |
| Median (IQR) time to onset of first ICANS event from last prior tarlatamab administration after each dose                                                                                                                                                                 | 3 days (1–7)               |               |         |         |         |
| Median (IQR) time to resolution of ICANS presenting as muscular weakness                                                                                                                                                                                                  | 69 days (42–not estimable) |               |         |         |         |
| Median (IQR) time to resolution of ICANS events excluding muscular weakness                                                                                                                                                                                               | 8 days (3–33)              |               |         |         |         |
| Median (IQR) resolution time of ICANS (Kaplan Meier estimate)                                                                                                                                                                                                             | 33 days (4–93)             |               |         |         |         |
| <sup>a</sup> Patients in parts 1 and 2 of the trial (n = 99) were monitored for 48 hours after tarlatamab infusion in cycle 1. Patients in part 3 (n = 34) were monitored for 24 hours during cycle 1 after tarlatamab after infusion.                                    |                            |               |         |         |         |
| <sup>b</sup> Hospitalization was not required for cycle 1 day 15 doses unless the patient experienced any grade CRS or neurological events following cycle 1 day 1 or cycle 1 day 8 doses in which case a 48h-hospitalization was required following cycle 1 day 15 dose. |                            |               |         |         |         |
| CRS: cytokine release syndrome; ICANS: immune-effector cell-associated neurotoxicity syndrome and associated neurological events; IQR, interquartile range                                                                                                                |                            |               |         |         |         |



# ICANS Grading and Management

| ICANS Grade <sup>a</sup> | Defining Symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                                | Management                                                                                                                                                                                                                                                                                                                                                                                               | Dose Modification                                                                                                                                                                                                                                                                                                                     |
|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grade 1                  | ICE score 7–9 <sup>c</sup> with no depressed level of consciousness                                                                                                                                                                                                                                                                                                                                                                                              | <ul style="list-style-type: none"> <li>Consider diagnostic work-up for alternative diagnosis</li> <li>Supportive care</li> </ul>                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>No treatment interruption needed</li> </ul>                                                                                                                                                                                                                                                    |
| Grade 2                  | ICE score 3–6 <sup>c</sup> and/or mild somnolence awakening to voice                                                                                                                                                                                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>Manage as for grade 1</li> <li>Dexamethasone<sup>b</sup> 10 mg IV (can repeat every 6 hours) or methylprednisolone 1 mg/kg IV every 12 hours if symptoms worsen</li> </ul>                                                                                                                                                                                        | <ul style="list-style-type: none"> <li>No treatment interruption needed</li> </ul>                                                                                                                                                                                                                                                    |
| Grade 3                  | ICE score 0–2 <sup>c</sup> and/or depressed level of consciousness awakening only to tactile stimulus and/or any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention and/or focal or local edema on neuroimaging                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Manage as for grade 2</li> <li>ICU care</li> <li>Consider mechanical ventilation for airway protection</li> <li>Dexamethasone<sup>b</sup> 10 mg IV every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours</li> <li>Consider repeat neuroimaging (CT or MRI) every 2–3 days if the patient has persistent grade ≥ 3 neurotoxicity</li> </ul>                | <ul style="list-style-type: none"> <li>Interrupt tarlatamab for at least 3 days and until the initial event improves to grade ≤ 1, then restart tarlatamab</li> <li>If there is no improvement to grade ≤ 1 within 7 days or grade 3 toxicity re-occurs within 7 days of re-initiation, permanently discontinue tarlatamab</li> </ul> |
| Grade 4                  | ICE score 0 <sup>c</sup> (patient is unarousable and unable to perform ICE) and/or stupor or coma and/or life-threatening prolonged seizure (> 5 minutes) or repetitive clinical or electrical seizures without return to baseline in between and/or deep focal motor weakness such as hemiparesis or paraparesis and/or diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing or papilledema, cranial nerve VI palsy, or Cushing's triad | <ul style="list-style-type: none"> <li>Manage as for grade 3</li> <li>ICU care</li> <li>Consider mechanical ventilation for airway protection</li> <li>High-dose corticosteroids<sup>b</sup></li> <li>Consider repeat neuroimaging (CT or MRI) every 2–3 days if the patient has persistent grade ≥ 3 neurotoxicity</li> <li>Treat convulsive status epilepticus per institutional guidelines</li> </ul> | <ul style="list-style-type: none"> <li>Permanently discontinue tarlatamab</li> </ul>                                                                                                                                                                                                                                                  |

## ICE Assessment Tool

| Task                                                                                                                                                                                   | Details                                                                                                      | Number of points |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|------------------|
| Orientation                                                                                                                                                                            | Orientation to year, month, city, hospital                                                                   | 4 points         |
| Naming                                                                                                                                                                                 | Ability to name 3 objects (eg, point to clock, pen, button)                                                  | 3 points         |
| Following commands                                                                                                                                                                     | Ability to follow simple commands (eg, "Show me two fingers" or "Close your eyes and stick out your tongue") | 1 point          |
| Writing                                                                                                                                                                                | Ability to write a standard sentence (eg, "Our national bird is the bald eagle")                             | 1 point          |
| Attention                                                                                                                                                                              | Ability to count backwards from 100 by 10                                                                    | 1 point          |
| Score interpretation: 10, no impairment; 7–9, grade 1 ICANS; 3–6, grade 2 ICANS; 0–2, grade 3 ICANS; 0, if patient is unarousable and unable to perform ICE assessment, grade 4 ICANS. |                                                                                                              |                  |
| ICE: immune effector cell-associated encephalopathy; ICANS: immune effector cell-associated neurotoxicity syndrome.                                                                    |                                                                                                              |                  |

Lee DW et al. *Biol Blood Marrow Transplant*. 2019;25(4):625–638.

# To Consider...

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Facilities and staff</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <ul style="list-style-type: none"> <li>• Infusion in specialized centers with a capacity for inpatient care.</li> <li>• Rapid access to a dedicated intermediate/ICU bed during the time period when the patient is at greatest risk of developing CRS (typically the first two doses of tarlatamab)</li> <li>• Adequate number of staff for post-infusion, vital sign monitoring<sup>b</sup></li> </ul>                                                                                                                                              |
| <b>Education</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <ul style="list-style-type: none"> <li>• Educate patients on symptom recognition for CRS and ICANS</li> <li>• Educate health care providers (doctors, nurses, staff at local emergency centers and ICUs) on T-cell engager-specific adverse event recognition and management</li> <li>• Educate patients and caregivers in keeping a diary that provides a descriptive record of symptoms, timing, and duration of AEs</li> </ul>                                                                                                                     |
| <b>Protocol</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <ul style="list-style-type: none"> <li>• Develop an institution- and drug-specific management protocol that can be readily accessed by all health care personnel involved in patient care</li> <li>• Develop protocol for adapting premedication and postmedication doses and monitoring depending on prior patient history of adverse events with the drug</li> </ul>                                                                                                                                                                                |
| <b>Medication</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | <ul style="list-style-type: none"> <li>• In addition to protocol-mandated premedication, ready access to at least two doses of tocilizumab to treat grade <math>\geq 2</math> CRS quickly, if needed</li> </ul>                                                                                                                                                                                                                                                                                                                                       |
| <b>Other considerations</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | <ul style="list-style-type: none"> <li>• Start infusion as early in the morning as possible to allow for longer patient monitoring by the main day shift</li> <li>• Development of a detailed handover protocol for the night-shift staff</li> <li>• Coordination with pharmacy for optimal drug delivery</li> <li>• Develop refined toxicity management protocols to define parameters for outpatient setting similar to that used with CAR-T therapies</li> <li>• Provide patients with a wallet card containing key contact information</li> </ul> |
| <p><sup>a</sup> Although not included in the DeLLphi-301 study protocol, some investigator-suggested considerations for management of CRS and ICANS are listed. These considerations were based on personal clinical experience and clinicians should use their own independent medical judgement for their individual patient's circumstances</p> <p><sup>b</sup> Refer to Supplementary Table 8 for the frequency of post-infusion patient monitoring</p> <p>CAR: chimeric antigen receptor; CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome and associated neurological events; ICU: intensive care unit.</p> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

Important to make sure any patient that needs tocilizumab gets it.

Wallet card provided to patients with contact information in case they end up in ER anywhere

# Review of Best Practices in operationalizing Tarlatamab from Pharmacy perspective

**Presenter:** Leila Rostamnjad, Pharm.D, BCOP

- Operational consideration
  - Site of Care
  - Transition of care
  - Patient access
  - Development of standardized monitoring and management
  - Staff education
  - Patient/Care giver education
  - Financial toxicity



# Pharmacist Responsibilities

## Drug on-boarding

- Pharmacy & Therapeutics committee presentation
- Beacon Plan built review
- Drug preparation and compounding workflow
- Development of standardized institutional toxicity management guidelines
- Development of infusion pharmacy and nursing
- Development of educational materials for patient and caregivers
- Patient education prior to drug administration

# Development of Toxicity Management and Prevention

- Institution Protocol Development
  - CRS and ICANS grading definitions
  - CRS and ICANS monitoring
  - CRS and ICANS management
- Supportive Care Medication Availability
  - CRS treatment may require tocilizumab
  - Institutions should have at least 2 tocilizumab doses available at all times

## Management of Cytokine Release Syndrome Related to Bispecific Antibodies

|                                        |                                                                                                                                                   |
|----------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|
| Sites Where Clinical Guideline Applies | All DFCI Ambulatory Sites                                                                                                                         |
| This Clinical Guideline Applies to     | Adults                                                                                                                                            |
| Target Audience                        | Providers, Pharmacists, and Nurses                                                                                                                |
| Description                            | This guideline provides guidance on service-specific ambulatory interventions for cytokine release syndrome resulting from bispecific antibodies. |

**Bispecific antibodies** can lead to an overactivation of the immune system, causing the release of large amounts of cytokines. This is known as a cytokine storm and leads to an acute systemic inflammatory syndrome, known as cytokine release syndrome (CRS).

This management guide is for commercial products only. For patients on a clinical trial, **FOLLOW PROTOCOL GUIDELINES FOR CRS MANAGEMENT.**

| CRS Grade | Clinical Presentation                                                                                         | Ambulatory Interventions                                                                                                                                                                                                                                                                                                                                                                                     |
|-----------|---------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| I         | Fever (Temperature $\geq 100.4^{\circ}\text{F}$ ) with or without headache, fatigue, nausea, myalgia, malaise | <ul style="list-style-type: none"><li>• Critical value VS (temperature <math>\geq 100.4^{\circ}\text{F}</math>) should be reported immediately to the treating provider (either APP or MD)</li><li>• If CRS is suspected, it is appropriate to have a provider assess the patient at the chairside to rule out other causes (e.g., hypersensitivity reactions, infections, etc.) and to develop an</li></ul> |

# Infusion Pharmacy and Nursing Education

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## At-a-Glance

### Tarlatamab-dlle (IMDELLTRA™)

Consult complete prescribing information and/or P&T drug monograph before prescribing, preparation, or administration. This document is created at the time of drug approval and is based on the prescribing information at that time. It is intended to provide a brief overview of the drug as initial education upon approval by P&T. It is not routinely reviewed or revised.

|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                  |                   |             |                     |
|-------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|-------------|---------------------|
| <b>Therapeutic Use/Indication</b>   | Treatment of adults with extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy.                                                                                                                                                                                                                                                                      |                   |             |                     |
| <b>Mechanism of Action</b>          | Bispecific delta-like ligand 3 (DLL3)-directed CD3 Tcell engager that binds to both DLL3 on tumor cells and CD3 on T cells, activating T cells to kill DLL3-expressing SCLC cells. This results in the formation of a cytolytic synapse with lysis of the cancer cell. DLL3 is a protein that is expressed on majority of SCLC cells, but is minimally expressed on healthy cells, making it an exciting target. |                   |             |                     |
| <b>Dose</b>                         | <b>Dosing Schedule</b>                                                                                                                                                                                                                                                                                                                                                                                           | <b>Day</b>        | <b>Dose</b> | <b>Cycle Length</b> |
|                                     | Step-up Dosing Schedule Cycle 1                                                                                                                                                                                                                                                                                                                                                                                  | Day 1 (inpatient) | 1 mg        | 28 days             |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                  | Day 8 (inpatient) | 10 mg       |                     |
|                                     |                                                                                                                                                                                                                                                                                                                                                                                                                  | Day 15            | 10 mg       |                     |
|                                     | Cycle 2                                                                                                                                                                                                                                                                                                                                                                                                          | Days 1 and 15     | 10 mg       | 28 Days             |
|                                     | Cycle 3 and 4                                                                                                                                                                                                                                                                                                                                                                                                    | Days 1 and 15     | 10 mg       | 28 Days             |
|                                     | Cycle 5 and subsequent infusions                                                                                                                                                                                                                                                                                                                                                                                 | Days 1 and 15     | 10 mg       | 28 Days             |
| Restarting therapy after dose delay |                                                                                                                                                                                                                                                                                                                                                                                                                  |                   |             |                     |

# Patient and Caregiver Education



**Dana-Farber**  
Cancer Institute

**Tarlatamab (Imdelltra)**

## **Immunotherapy: Tarlatamab-dlle (Imdelltra™)**

Pronounced: *"Tar-la-ta-mab"*

**How medicine is given:** By vein (IV)

**Purpose:** To treat extensive stage small cell lung cancer (ES-SCLC)

### **Before treatment:**

- Tell your cancer care team if you are sick or have an infection. Infections can cause severe, life-threatening illness while you are receiving this medicine.

### **Things that may occur during or within hours of treatment**

During the time that you get tarlatamab-dlle, and even several days later, you may have a serious reaction.



# Patient and Caregiver Education

- Educate patients and caregivers about potentially life-threatening side effects of tarlatamab such as:
  - Cytokine release syndrome (CRS)
  - Immune effector cell-associated neurotoxicity syndrome (ICANS)
- Educate caregivers regarding their essential role in the first 10 days of tarlatamab treatment.
  - Monitoring vital signs multiple times a day
  - Recognizing signs of neurotoxicity.
- Reinforce the importance of adhering to the treatment plan, attending all appointments, and following the guidelines for monitoring and reporting side effects.

# Education of Medical Staff

- Identify key stakeholders among medical staff
  - Core care team – who will be prescribing and/or following up with patients to prevent and manage complications on a scheduled basis?
    - Oncologists, advanced practice providers, clinical pharmacists, clinical nurse coordinators/care coordinators
  - Dispensing pharmacists, technicians (inpatient and ambulatory/infusion)
  - Bedside nurses (inpatient, infusion, critical care)
  - Scheduling team
  - Inpatient care staff and after-hours care teams
  - Emergency, critical care, neurology providers
- Recognize opportunities for formal education for medical staff

## Dosing and Administration and Monitoring

| Drug       | Dose | Dose Units | Route | Schedule                | Cycle Length |
|------------|------|------------|-------|-------------------------|--------------|
| Tarlatamab | 1    | mg         | IV    | C1D1                    | 28 days      |
|            | 10   | mg         | IV    | C1D8 , C1D15            | 28 days      |
|            | 10   | mg         | IV    | C2D1 , C2D15 and beyond | 28 days      |

| Drug       | Dose | Dose Units | Schedule              | Monitoring                                               |
|------------|------|------------|-----------------------|----------------------------------------------------------|
| Tarlatamab | 1    | mg         | C1D1                  | 22-24 hours (inpatient admission) from start of infusion |
|            | 10   | mg         | C1D8                  |                                                          |
|            | 10   | mg         | C1D15*                | 6-8 hours post infusion                                  |
|            | 10   | mg         | C2D1 , C2D15*         |                                                          |
|            | 10   | mg         | C3 D1, C3D15*         | 3-4 hours post infusion                                  |
|            | 10   | mg         | C4D1,C4D15*           |                                                          |
|            | 10   | mg         | C5D1,C5D15 and beyond | 2 hours post infusion                                    |

\*Extended monitoring if patient experiences Grade  $\geq 2$  CRS, ICANS or neurological toxicity during prior treatments

- Reginal campus Administration: C3 and beyond

# Overview of Phases of Care

## **OUTPATIENT**

Patient Identified as a candidate for Tarlatamab therapy by oncologist

## **INPATIENT**

Patient admitted for dose per manufacturer guidance for closer monitoring and interventions if needed for CRS, neurologic toxicity

## **OUTPATIENT**

Patient is discharged back to primary oncologist for subsequent Tarlatamab doses and follow-up

## **INPATIENT**

If a subsequent dose is delayed or a serious complication arises, patient maybe readmitted for drug administration and/or elevated level of cares

# Pre-Admission

- Attainment of patient consent, baseline labs before admission
- Collaboration to ensure insurance authorization for inpatient admission and subsequent outpatient doses to prevent delays in care
- Communication of standardized post-discharge processes
- What does follow-up (including in-person, telephone, and/or telehealth visits) entail?
- Which discharge prophylactic medications if any are required?
- What is the appropriate contact information for toxicity assessment (including after-hours triaging)?
- Patient/caregiver education and **drug card**

# Monitoring Standardization & Handoff

- Monitoring standardization
  - Important for transitions between inpatient care settings AND inpatient/outpatient settings
  - Nursing flow sheet for CRS/ICANS monitoring
- Handoff between sites of care
  - Doses administered
  - Premedications prior to previous dose
  - CRS/ICANS grading with treatments administered if needed

# Community/Rural Considerations

- Assess institutional capabilities for after-hours coverage
- Weekend or overnight staffing coverage (triaging, assessment, treatment, referral)
- Specialists (e.g., neurologists) readily accessible at core team's or partner institution?
- Local institutions for emergency assessment/treatment?
- Telehealth visits if patient is stable on therapy
- Patient eligibility for home health services
- Share patient resources, such as local and/or virtual patient support groups

# In Summary:

- Recommend institution-driven practice guidelines/protocols to standardize toxicity management
- Collaborate with available institutions and medical staff teams to provide knowledgeable, comprehensive care for patients, especially to optimize transitions of care
- Approach financial challenges and unique operational requirements from a variety of angles
- Consider clinical characteristics, socioeconomic factors, and accessibility when selecting patient

# Inpatient Program Implementation Process

**Presenter:** Kara Stocks, PA-C

- Institutional policy development
- Hospital and inpatient implementation challenges
- Logistical hurdles and coordination
- Identifying champions for program leadership
- Strategies for gaining hospital administrative approval (Laura House)
- Identifying workforce and training for successful implementation

# Institutional Policy Development

- DFCI/BWH Inpatient Cancer center is a large academic medical center, therefore many policies and procedures are already in place for both inpatient clinical trials and standard of care drugs
- Majority of inpatient oncology trials have fallen on the hematology malignancy teams, we were able to use their teams as a resource for policy development

# Hospital and Inpatient Implementation Challenges

- Prep work: assuring there was adequate education once drug became standard of care, transitioning from clinical trial to standard of care
- Education: educating nursing (day and night shift), attendings, RCs (PAs/NP/residents), nocturnist pool, pharmacy
- Rescue drug stock: ensuring adequate hospital supply of toci
- Drug timing: Initially timed drug administration for evening so that CRS most likely to occur during day shift, however this lead to patients waiting for drug and also waiting to be discharged

# Logistical Hurdles

- BWH/DFCI has dedicated research floor which had planned to take Tarlatamab patients however census constraints lead to the need for admission to any floor, and therefore a need for more widespread education
- Admission capability in a large academic medical center, ensuring subsequent admissions can be booked appropriately
- Providers not always comfortable making decision about toci, therefore someone from the outpatient teams always needing to be available for guidance

# Identifying Champions In Program Leadership

- Nurse Director of Inpatient Oncology Research Program
- Inpatient Clinical Research PA
- Inpatient Chief Solid Tumor PA Program
- Collaboration with the outpatient team

# Identifying workforce and training for successful implementation

- Dr. Sands presented to RCs, hospitalist group, and nocturnists prior to drug roll out
- RCs provided with summary and guidelines for CRS/ICANS management
- Collaboration between ambulatory and inpatient service regarding discharge education. This has helped to streamline education on discharge and identify outpatient needs (additional inpatient cycle, level of outpatient monitoring)

# Real-World Application and Case Studies

- **Content:**

- Case studies of T-Cell Engager Therapy in practice
- Focus on CRS (Cytokine Release Syndrome) and ICANS (Immune Effector Cell-Associated Neurotoxicity Syndrome)
- Multidisciplinary collaboration on care pathways
- Lessons learned and discussion on improvements

# Case Study #1

## Cytokine Release Syndrome

# Case Presentation

- 63-year-old female former smoker diagnosed with extensive stage SCLC in 11/2023
- 11/2023: Started on etoposide/carboplatin + atezolizumab
- 05/2024: Developed disease progression
- 06/2024: Started on 2<sup>nd</sup>-line lurbinectedin
- 09/2024: Developed disease progression
- 10/2024: **Initiated** 3<sup>rd</sup>-line tarlatamab
  - Bispecific T-cell Engager (BiTE therapy)
  - 22-24 hour observation for first 2 treatments due to risk of CRS

# Case Presentation ( Cont.)

- Patient gets C1D1 of tarlatamab 1 mg inpatient hospital
  - During initial observation receives standard 8 hours of IVF and monitoring, vital signs are unremarkable
- At 18 hours, patient develops fever of 100.7
- No infectious symptoms
- Vital signs are WNL

**What would you do 4 hours later if fever persists?**

# CRS Grading and Management

| CRS Grade | Defining Symptoms                                                                                                                                                                                                                                                                                       | Management <sup>a</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grade 1   | Fever $\geq 38^{\circ}\text{C}$ , without hypotension or hypoxia                                                                                                                                                                                                                                        | <ul style="list-style-type: none"> <li>Symptomatic treatment (e.g., paracetamol/acetaminophen) for fever</li> <li>Culture, if neutropenic cover w/ abx</li> </ul>                                                                                                                                                                                                                                                                                                                                                                 |
| Grade 2   | <ul style="list-style-type: none"> <li>Fever <math>\geq 38^{\circ}\text{C}</math>,</li> <li>Hypotension not requiring vasopressors, and/or</li> <li>Hypoxia requiring low-flow nasal cannula</li> </ul>                                                                                                 | <ul style="list-style-type: none"> <li>Supplemental oxygen when oxygen saturation <math>&lt; 90\%</math> on room air</li> <li>Intravenous fluids when SBP <math>&lt; 85</math> mmHg and/or persistent tachycardia (heart rate <math>&gt; 120</math> bpm) or symptomatic (eg dizziness/lightheadedness)</li> <li>If not responding to fluids, page oncologist and given Dex 8-10 mg</li> <li>If not responding to dex (give about an hour) then consider Tocilizumab (dose is 8mg/kg). Expect to take 1 hour to kick in</li> </ul> |
| Grade 3   | Severe symptoms defined as temperature $\geq 38^{\circ}\text{C}$ with: <ul style="list-style-type: none"> <li>HD instability requiring a vasopressor) or</li> <li>Worsening hypoxia or respiratory distress requiring high-flow nasal canula (<math>&gt; 6</math> L/min oxygen) or face mask</li> </ul> | <ul style="list-style-type: none"> <li>Supplemental oxygen</li> <li>Vasopressor <math>\pm</math> vasopressin</li> <li>IV Dexamethasone (or equivalent), and/or</li> <li>Tocilizumab, can consider additional dose but would need to discuss further</li> </ul>                                                                                                                                                                                                                                                                    |
| Grade 4   | Fever (Temp $\geq 38^{\circ}\text{C}$ ) WITH Hypotension (requiring multiple vasopressors, excluding vasopressin) And/Or Hypoxia (requiring positive pressure, not attributable to another cause)                                                                                                       | <ul style="list-style-type: none"> <li>Intensive monitoring, e.g., ICU care</li> <li>See Grade I, II and III for supportive care</li> <li>Tocilizumab 8 mg/kg IV may be administered per provider discretion</li> </ul>                                                                                                                                                                                                                                                                                                           |

Lee DW et al. *Biol Blood Marrow Transplant.* 2019;25(4):625-638.

## Practical Management of Adverse Events in Patients Receiving Tarlatamab, a DLL3-targeted Bispecific T-cell Engager Immunotherapy, for Previously Treated Small Cell Lung Cancer

**Running Title:** Tarlatamab adverse event management

Jacob M. Sands MD<sup>1†</sup>, Stéphane Champiat MD, PhD<sup>2\*†</sup>, Horst-Dieter Hummel MD<sup>3</sup>, Kelly G. Paulson MD, PhD<sup>4</sup>, Hossein Borghaei DO<sup>5</sup>, Jean Bustamante Alvarez MD<sup>6</sup>, David P. Carbone MD, PhD<sup>7</sup>, Jennifer W. Carlisle MD<sup>8</sup>, Noura J. Choudhury MD<sup>9†</sup>, Jeffrey M. Clarke MD<sup>10</sup>, Shirish M. Gadgeel MD<sup>11</sup>, Hiroki Izumi MD, PhD<sup>12</sup>, Alejandro Navarro MD<sup>13</sup>, Sally C. M. Lau MD<sup>14</sup>, Philip E. Lammers MD<sup>15</sup>, Shuang Huang PhD<sup>16</sup>, Ali Hamidi MD<sup>16</sup>, Sujoy Mukherjee MD<sup>16</sup>, Taofeek K. Owonikoko MD, PhD<sup>17</sup>

# Case Presentation (Cont.)

- Fever resolved in 24 hours; no other symptoms developed
- Infectious work up was unremarkable
- Patient is sent home with instructions to evaluate for SOB/hypoxia, tachycardia, hypotension, or worsening fever and should call and come to be seen if any of those develop.
  - **Discuss the importance of the ONN role post hospital discharge.**
- Patient now comes in 7 days later for C1D8 of tarlatamab at step-up dose of 10 mg IV
  - **What dose would you give the patient: the 10 mg or the 1 mg?**

# Conclusions

- Understand CRS grading and treatment
- Be sure inpatient team also understands this and has good line of communication with outpatient team
- CRS with tarlatamab is rarely more than grade 2, usually can be managed and resolved in a matter of days.
- Wallet Card



Case Study #2

Immune Effector Cell Associated Neurotoxicity  
Syndrome (ICANS)

DO NOT SHARE

# Case Presentation

- 59-year-old female with history of hypothyroidism, anxiety, hypertension, and 45 pack-year smoking history diagnosed with ES-SCLC
- Course complicated by CNS involvement s/p WBRT
- Started tarlatamab with uncomplicated inpatient stay, but now presents for C2D1 tarlatamab with new symptoms including dizziness, forgetfulness, slow thinking, and generalized muscle weakness causing balance issues

# Case Presentation (Cont.)

59-year-old female with ES-SCLC presents for C2D1 tarlatamab with dizziness, forgetfulness, slow thinking, and generalized weakness causing balance issues

- Hemodynamically stable
- Lab work unremarkable
- ICE Score completed: 8/10 (month, counting backward)
- No Change in LOC
- Grade 1 ICANS

**How should we best manage her care?**

# ICANS Grading and Management

| ICANS Grade <sup>a</sup> | Defining Symptoms                                                                                                                                                                                                                                                                                                                                                                                                                                                | Management                                                                                                                                                                                                                                                                                                                                                                                               | Dose Modification                                                                                                                                                                                                                                                                                                                     |
|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Grade 1                  | ICE score 7–9 <sup>c</sup> with no depressed level of consciousness                                                                                                                                                                                                                                                                                                                                                                                              | <ul style="list-style-type: none"> <li>Consider diagnostic work-up for alternative diagnosis</li> <li>Supportive care</li> </ul>                                                                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>No treatment interruption needed</li> </ul>                                                                                                                                                                                                                                                    |
| Grade 2                  | ICE score 3–6 <sup>c</sup> and/or mild somnolence awakening to voice                                                                                                                                                                                                                                                                                                                                                                                             | <ul style="list-style-type: none"> <li>Manage as for grade 1</li> <li>Dexamethasone<sup>b</sup> 10 mg IV (can repeat every 6 hours) or methylprednisolone 1 mg/kg IV every 12 hours if symptoms worsen</li> </ul>                                                                                                                                                                                        | <ul style="list-style-type: none"> <li>No treatment interruption needed</li> </ul>                                                                                                                                                                                                                                                    |
| Grade 3                  | ICE score 0–2 <sup>c</sup> and/or depressed level of consciousness awakening only to tactile stimulus and/or any clinical seizure focal or generalized that resolves rapidly or nonconvulsive seizures on EEG that resolve with intervention and/or focal or local edema on neuroimaging                                                                                                                                                                         | <ul style="list-style-type: none"> <li>Manage as for grade 2</li> <li>ICU care</li> <li>Consider mechanical ventilation for airway protection</li> <li>Dexamethasone<sup>b</sup> 10 mg IV every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours</li> <li>Consider repeat neuroimaging (CT or MRI) every 2–3 days if the patient has persistent grade ≥ 3 neurotoxicity</li> </ul>                | <ul style="list-style-type: none"> <li>Interrupt tarlatamab for at least 3 days and until the initial event improves to grade ≤ 1, then restart tarlatamab</li> <li>If there is no improvement to grade ≤ 1 within 7 days or grade 3 toxicity re-occurs within 7 days of re-initiation, permanently discontinue tarlatamab</li> </ul> |
| Grade 4                  | ICE score 0 <sup>c</sup> (patient is unarousable and unable to perform ICE) and/or stupor or coma and/or life-threatening prolonged seizure (> 5 minutes) or repetitive clinical or electrical seizures without return to baseline in between and/or deep focal motor weakness such as hemiparesis or paraparesis and/or diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing or papilledema, cranial nerve VI palsy, or Cushing's triad | <ul style="list-style-type: none"> <li>Manage as for grade 3</li> <li>ICU care</li> <li>Consider mechanical ventilation for airway protection</li> <li>High-dose corticosteroids<sup>b</sup></li> <li>Consider repeat neuroimaging (CT or MRI) every 2–3 days if the patient has persistent grade ≥ 3 neurotoxicity</li> <li>Treat convulsive status epilepticus per institutional guidelines</li> </ul> | <ul style="list-style-type: none"> <li>Permanently discontinue tarlatamab</li> </ul>                                                                                                                                                                                                                                                  |

## ICE Assessment Tool

| Task                                                                                                                                                                                   | Details                                                                                                      | Number of points |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------|------------------|
| Orientation                                                                                                                                                                            | Orientation to year, month, city, hospital                                                                   | 4 points         |
| Naming                                                                                                                                                                                 | Ability to name 3 objects (eg, point to clock, pen, button)                                                  | 3 points         |
| Following commands                                                                                                                                                                     | Ability to follow simple commands (eg, "Show me two fingers" or "Close your eyes and stick out your tongue") | 1 point          |
| Writing                                                                                                                                                                                | Ability to write a standard sentence (eg, "Our national bird is the bald eagle")                             | 1 point          |
| Attention                                                                                                                                                                              | Ability to count backwards from 100 by 10                                                                    | 1 point          |
| Score interpretation: 10, no impairment; 7–9, grade 1 ICANS; 3–6, grade 2 ICANS; 0–2, grade 3 ICANS; 0, if patient is unarousable and unable to perform ICE assessment, grade 4 ICANS. |                                                                                                              |                  |
| ICE: immune effector cell-associated encephalopathy; ICANS: immune effector cell-associated neurotoxicity syndrome.                                                                    |                                                                                                              |                  |

Lee DW et al. *Biol Blood Marrow Transplant*. 2019;25(4):625–638.

# Conclusions

- Education is key for early identification and symptom reporting from both patient and caregivers
- Be sure to understand ICANS grading and management
- Key is communication with medical team – multi-disciplinary approach
- ICANS with tarlatamab is rarely more than grade 2, usually can be managed and resolved within 1-2 weeks
- Wallet card – provided to patients with contact information in case they end up in ER anywhere

# Q&A Session



# Summary and Future Directions

**Presenter:** Dr. Jacob Sands

**Content:**

- Summary of key takeaways from the session
- Future directions in research and treatment advancements

# Helpful Resources

## Adverse Events Management Publication

Received: 30 September 2024 | Revised: 22 November 2024 | Accepted: 20 December 2024  
DOI: 10.1002/cncr.35738

### REVIEW ARTICLE

**Practical management of adverse events in patients receiving tarlatamab, a delta-like ligand 3–targeted bispecific T-cell engager immunotherapy, for previously treated small cell lung cancer**

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<https://pmc.ncbi.nlm.nih.gov/articles/PMC11775405/pdf/CNCR-131-0.pdf>

## Bispecific Agents in Solid Tumors Nurse Resource Guide

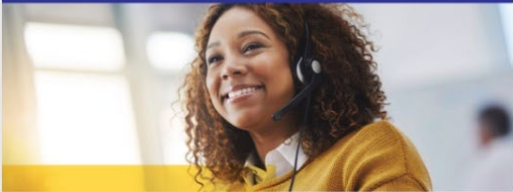


<https://aonn.site/zDfjaYVx>



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