Operationalization of Tarlatamab therapy at Moffitt Cancer Center

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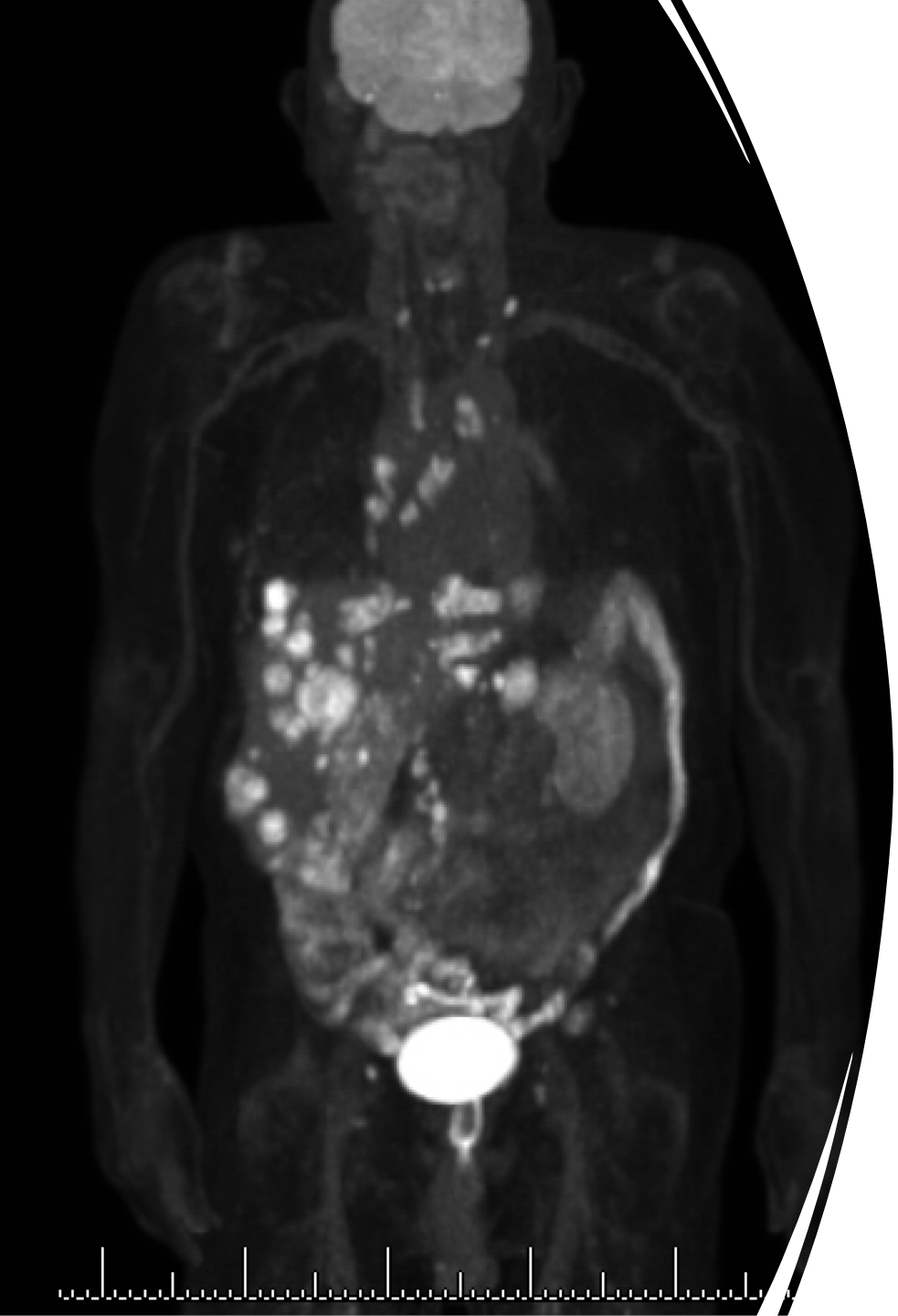
2025 Cell Coast Conference
17th October 2025

Disclosures

Ad board/ consulting –
BMS,
Novocure,
Oncohost,
Takeda,
Janssen,
Daiichi Sanko,
Amgen,
Astrazeneca,
Boehringer Ingelheim,
Immunity bio

Outline

- Introduction
- Operationalization of Tarlatamab therapy at MCC
- 17 months of SOC Tarlatamab: Lessons learnt
- Bridging the gap



Small Cell, Big Fight: Tackling the Reality of SCLC in the Clinic

- 15% of lung cancers are diagnosed as Small Cell Lung Cancer (SCLC)
- Highly aggressive malignancy
  - Majority of patients diagnosed with stage IV /endstage disease
  - Dismal prognosis with a 5-year survival of ~12%
- Although considered highly responsive to first line therapy, resistance to novel therapies like conventional immunotherapy is common
- Recurrence is inevitable!
- Subsequent lines of therapy historically with limited efficacy.

SCLC Treatment History: Recent Approvals

FDA approvals

2019
First-line platinum-etoposide-atezolizumab

2020
First-line platinum-etoposide-durvalumab

Second-line lurbinectedin

Supportive care trilaciclib

2021

2022

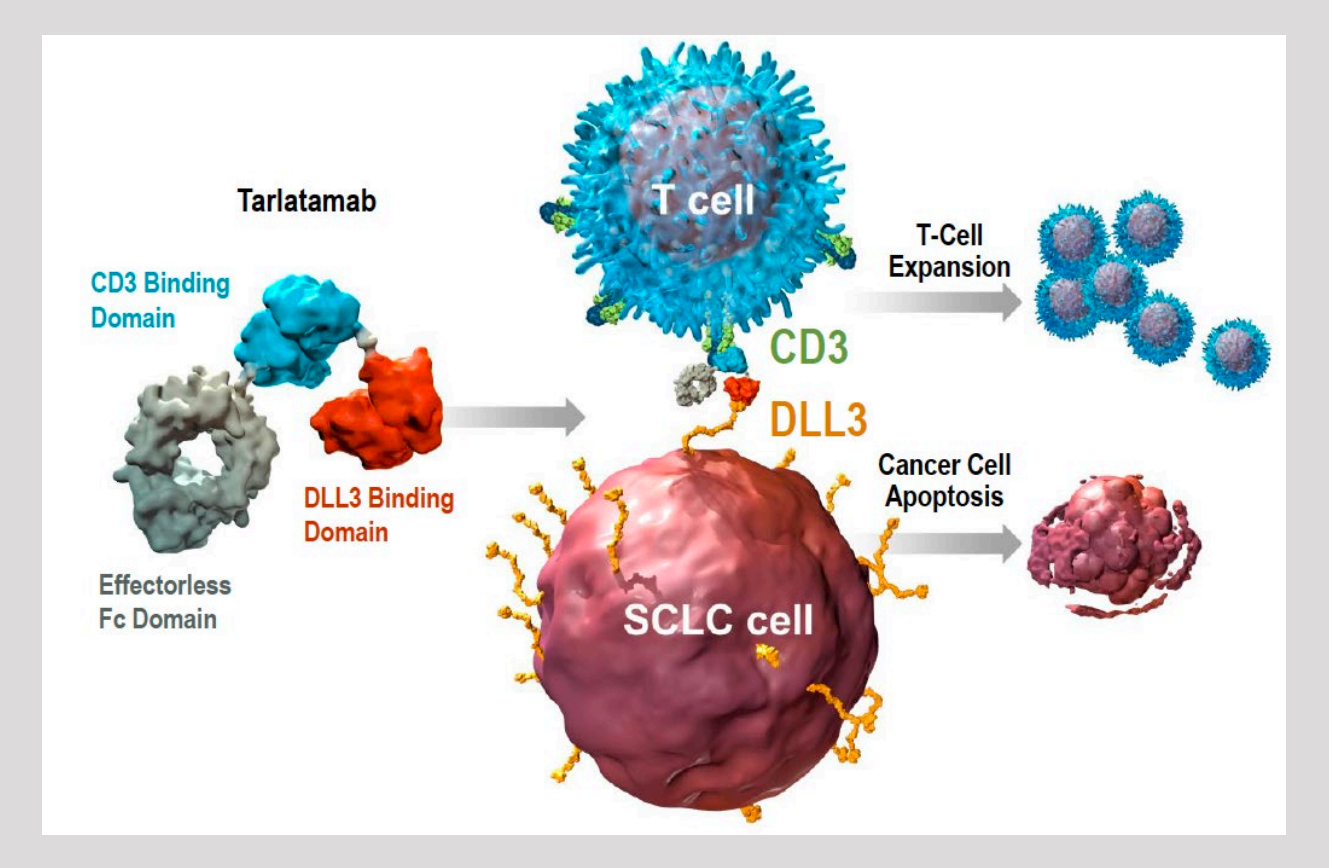
2023
Second-line Tarlatamab

Consolidation limited stage disease

Durvalumab

2024

Second-line Tarlatamab



Tarlatamab Efficacy: Redefining What's Possible in Small Cell Lung Cancer Care

Impressive response rates in heavily pre- treated SCLC

- Objective response rate: 40%
- Disease control rate: 70%

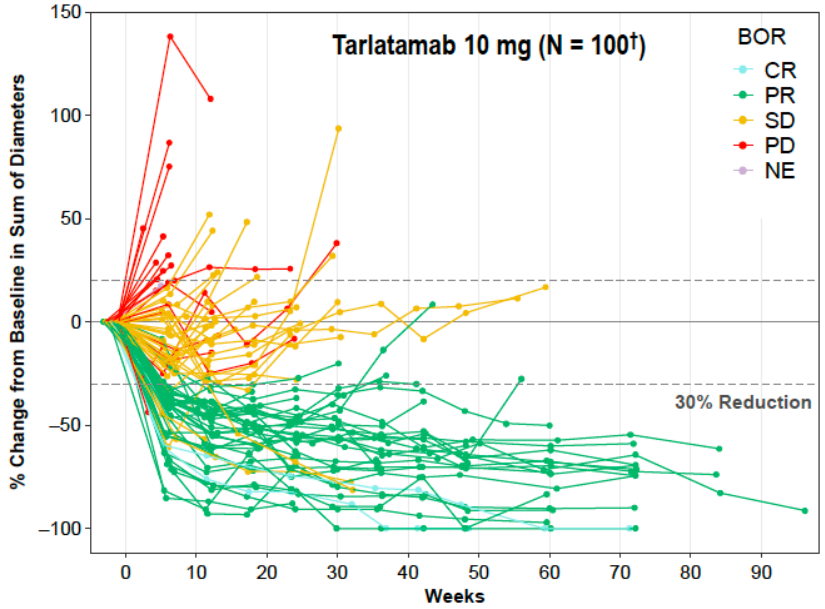
Durable response to therapy

- Median duration of response was 9.7 months

Promising survival benefit

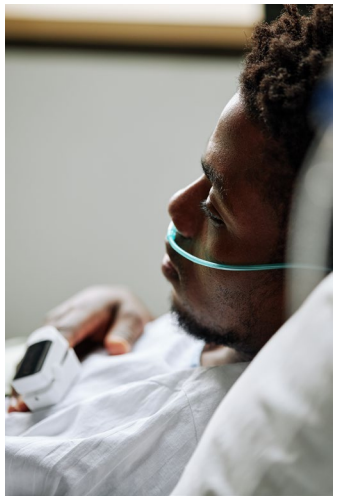
- Median overall survival 15.2 months

Sustained Disease Control*



Sands J. Presented at WCLC 2024

Tarlatamab Toxicity: Importance of Expertise and Close Monitoring



Cytokine Release Syndrome (CRS)

A potentially life-threatening side effect characterized by a systemic inflammatory response, including high fever, hypotension, and organ dysfunction. It is caused by the rapid release of large amounts of cytokines into the bloodstream.

Overall incidence with Tarlatamab 10mg dose ~ 50% mostly G1-2 with cycle 1

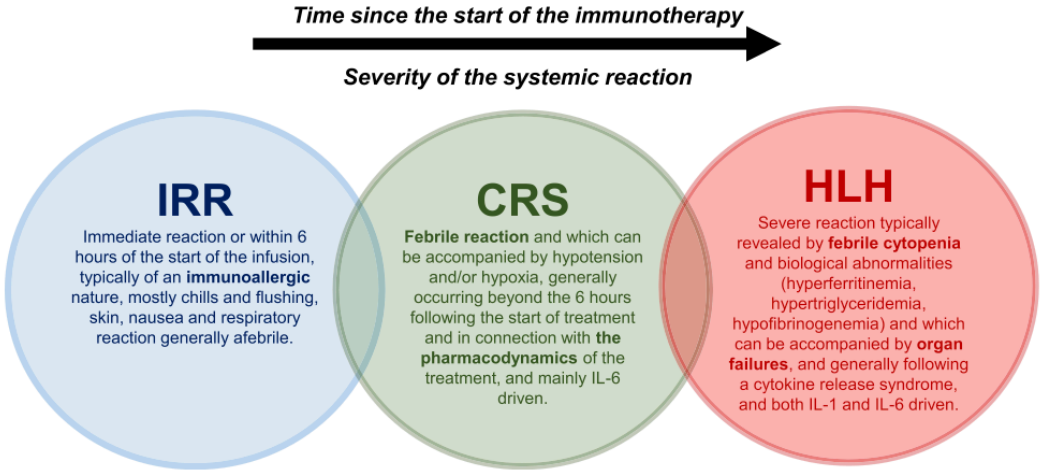
ICANS (Immune Effector Cell-Associated Neurotoxicity Syndrome)

A specific type of side effect that can occur with bispecific T-cell engagers, characterized by neurological symptoms such as altered mental status, seizures, and cerebral edema.

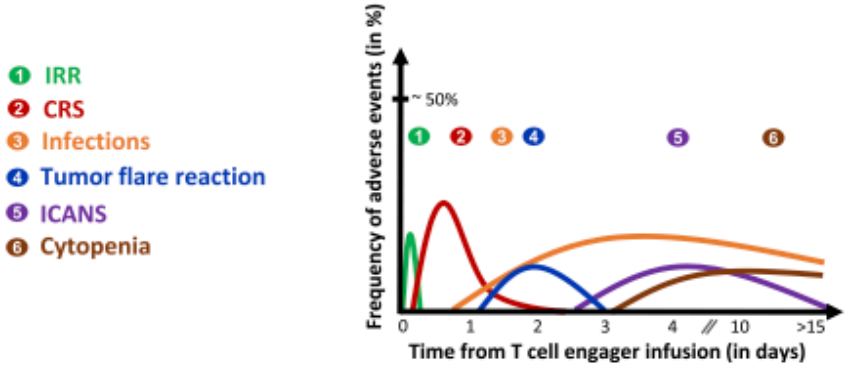
Overall incidence with Tarlatamab 10mg dose ~ 10% mostly G1-2 with cycle 1

Early identification and prompt management of these adverse events are crucial to prevent serious complications and ensure optimal patient outcomes.

Definition and distinctions points between the three main systemic drugs reactions related to anti-cancer immunotherapies.



Expected timing for reactions and adverse events with T-cell engagers



Both overdiagnosis and underdiagnosis of T cell Engager(TCE) therapy related toxicity- CRS and ICANS is a challenge

Key points for the management of reactions and adverse events with T-cell engagers

	IRR *with anaphylaxis*	IRR *without anaphylaxis*	CRS	Infections	Tumor flare reactions	ICANS	Cytopenia
Typical expected time of occurrence	Immediate, in first minutes of treatment, or at second administration	During the 6 first hours after starting infusion	4 – 16 hours after infusion	1-14 days after infusion	1-3 days after infusion	3-9 days after infusion	3-14 days after infusion
Main sign and symptoms	Anaphylaxis, hypotension, laryngeal angioedema, bronchospasm	Chills, flushing, moderate fever, urticaria, nausea, vomiting	Fever, hypotension, hypoxia	Fever, chills, viral or bacterial infections signs	Tumor pain, effusion worsening, tumor compression signs and symptoms.	Speech difficulties, behavior modification, memory trouble, confusion, headache, seizure.	Neutropenia, anemia, thrombocytopenia related symptoms.
Pathophysiology aspects	IgE mediated	Cytokine elevation, none-IgE mediated	Cytokine storm IL-6 mediated	On target effect in immune component	Tumor microenvironement inflammation	Endothelial and blood-brain barrier disturbances	Direct toxicity on hematopoietic precursor (mainly TCE for blood cancer)
Main drugs interventions	Epinephrin IM in life-threatening cases	H1/H2-receptor antagonists,acetaminophen, antileucotriens, corticosteroids, bronchodilators	Anti-IL6 receptor, corticosteroids, vasopressor in severe cases	Anti-infectious agents to treat infection. Prevention and pre-emptive measures are important with prophylaxis, vaccinations, gammaglobulins in severe cases with humoral deficiency	Corticosteroids, analgesic	Corticosteroids (dexamethasone preffered), non sedative anti-convulsant, antagoniste des récepteurs de l'interleukine-1 (IL-1ra) in severe cases	Stimulating factors (GCSF) for neutropenia

Gˊeraud et al. European Journal of Cancer 2024

Operationalization of Tarlatamab therapy at MCC

October 2023

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer

M.-J. Ahn, B.C. Cho, E. Felip, I. Korantzis, K. Ohashi, M. Majem, O. Juan-Vidal, S. Handzhiev, H. Izumi, J.-S. Lee, R. Dziadziuszko, J. Wolf, F. Blackhall, M. Reck, J. Bustamante Alvarez, H.-D. Hummel, A.-M.C. Dingemans, J. Sands, H. Akamatsu, T.K. Owonikoko, S.S. Ramalingam, H. Borghaei, M.L. Johnson, S. Huang, S. Mukherjee, M. Minocha, T. Jiang, P. Martinez, E.S. Anderson, and L. Paz-Ares, for the DeLLphi-301 Investigators*

December 2023

FDA GRANTS PRIORITY REVIEW TO AMGEN'S TARLATAMAB APPLICATION FOR ADVANCED SMALL CELL LUNG CANCER

Currently There are no Approved Therapeutic Options for Third-Line Treatment of Advanced SCLC[1]

If Approved, Tarlatamab Would be the First BiTE® Therapy for a Major Solid Tumor

FDA Target Action Date is June 12, 2024

May 16, 2024

FDA grants accelerated approval to tarlatamab-dlle for extensive stage small cell lung cancer

May 26, 2024

Moffitt is First in U.S. to Offer New Lung Cancer Therapy

By Pat Carragher - May 29, 2024

Moffitt Cancer Center has become the first health care provider in the United States to commercially treat a patient with extensive stage small cell lung cancer (SCLC) using the newly approved tarlatamab. The FDA approved the drug on May 16.

Moffitt Cancer Center Leading the Charge

KEY COMPONENTS

- Active tracker created for potentially eligible patients
- Scheduling algorithm updated to ensure these patients are flagged and scheduled within 3 days
- Nurse navigator and social worker assigned for patient follow-up.

- Collaboration between Thoracic Oncology and Inpatient Hematology teams·
- Identify and prepare treatment spaces

Regular communication with the specialty pharmacy and reimbursement team to facilitate establishment of pathways for rapid patient identification and prior authorization process

Create order sets and comprehensive multidisciplinary treatment protocols that outline patient selection criteria, dosing guidelines, administration procedures, and management of potential adverse events.

Patient Identification → **Establishment of a multidisciplinary team** → **Reimbursement** → **Development of Electronic medical record order sets and treatment protocols**

Provide ongoing staff training → **Establishment of triage system for monitoring of treatment related adverse events (AEs)** → **Patient Education and Support**

Conduct regular training sessions and assessments to ensure that all staff involved in Tarlatamab therapy administration maintain their knowledge and skills.

- Early identification of AEs concerning for cytokine release syndrome and immune effector cell mediated neurological symptoms.
- Establishment of Fast track assessment in the cancer center urgent care center

Develop educational materials and programs to inform patients about the therapy, its benefits, potential side effects, and self-management strategies.

17 months of SOC Tarlatamab : Lessons Learnt

The rewards ..

Tarlatamab for Large Cell Neuroendocrine Carcinoma in a Young Adult: A Case Report

Shetal A. Patel, MD, PhD [a,b] · Young Whang, MD, PhD [a,b] · Chaely Medley, NP [b] · ... · Dante Bortone, PhD [a] · Benjamin Vincent, MD, PhD [a] · Jared Weiss, MD [a,b] ... Show more

Affiliations & Notes Article Info

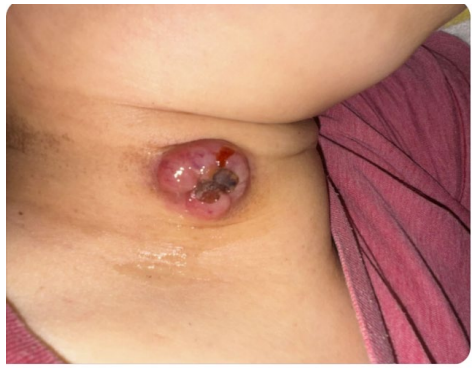
CASE REPORT · Articles in Press, March 24, 2025

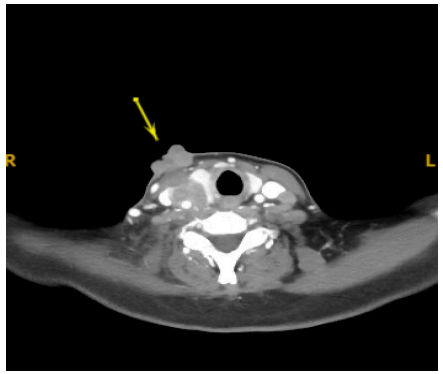
Rapid Intracranial Response With Tarlatamab in Patients With Untreated Brain Metastases From SCLC—A Real-World Case Series: Case Report

Bingnan Zhang, MD [a] · Komal B. Shah, MD [b] · Mitchell Parma, MD [c] · Kaiwen Wang, PharmD [d] · Eric K. Singhi, MD [a] · Whitney Lewis, PharmD [d] · Melvin Rivera, PharmD [d] · Mehmet Altan, MD [a] · Jenny Pozadzides, MD [a] · Xiuning Le, MD, PhD [a] · Natalie Vokes, MD [a] · Frank Fossella, MD [a] · Barbara O'Brien, MD [e] · Chenyang Wang, MD, PhD [f] · Martin C. Tom, MD [f] · Thomas Beckham, MD, PhD [f] · Todd Swanson, MD, PhD [f] · Julianna Bronk, MD, PhD [g] · Steven H. Lin, MD, PhD [g] · Maria Franco Vega, MD [h] · Joshua Jacome, MPAS [a] · Alexa Halliday, BSc [a] · Marcelo Negrao, MD [a] · Jianjun Zhang, MD, PhD [a] · Don L. Gibbons, MD, PhD [a] · John V. Heymach, MD, PhD [a] · Lauren A. Byers, MD [a] · Carl M. Gay, MD, PhD [a] Show less

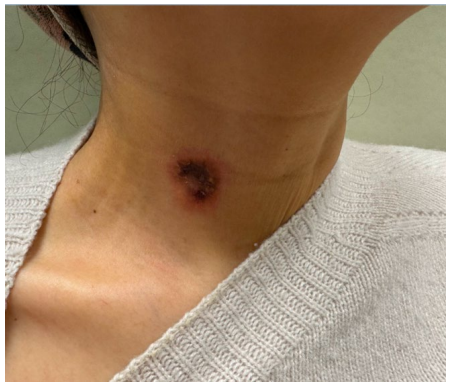
Activity in extra-pulmonary neuroendocrine tumors

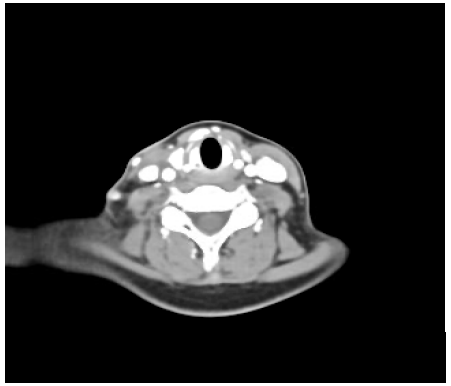
Pre-Infusion





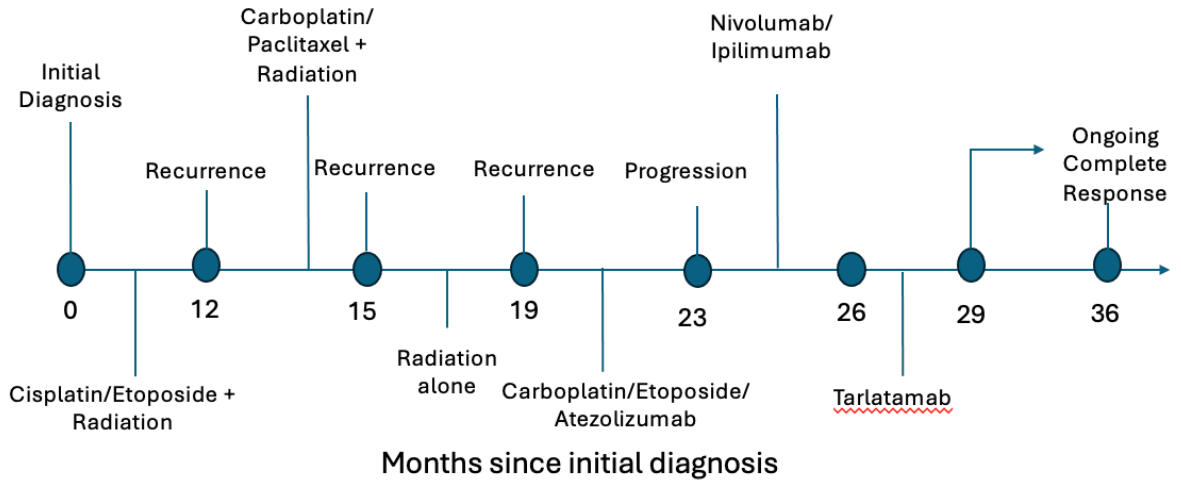
Post Cycle 2 (Complete Response):





A 45-year-old female with history of Small cell carcinoma of left pyriform sinus with cervical LAP , DLL3 (SP347, Ventana) 95%

Figure 2: Timeline of Treatment



Images courtesy : Dr Kedar Kirtane

Kirtane, Puri , Chung et al . Manuscript under review , JCO-PO

Some challenges ..

O'NEAL COMPREHENSIVE CANCER CENTER
THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Real-World Outcomes with Tarlatamab in Second-Line Setting and Beyond for Extensive Stage Small Cell Lung Cancer

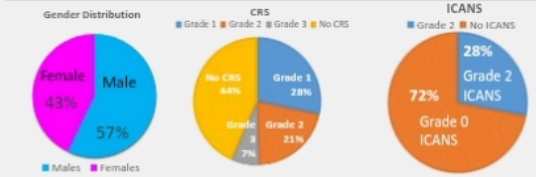
Mobile Infirmary
INFIRMARY HEALTH

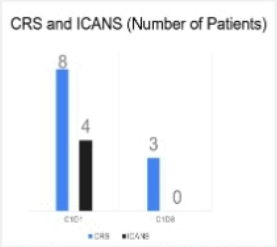
Authors: Sameer Deshmukh[1], Emmanuel Ekpenyong[2], Sanad Alhushki[1], Ellen McNeeley[1], Yanis Boumber[1], Maya Khalil[1], Selvarangan Ponnazhagan[1], Jan Kemnade[1,2], Aakash Desai[1]

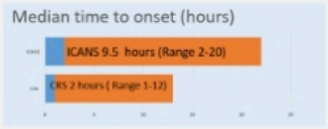
1 O'Neal Comprehensive Cancer Center at UAB School of Medicine, Birmingham, AL 2. Mobile Infirmary Medical Center, Mobile, AL

BACKGROUND

- **Tarlatamab**, a **CD3 × DLL3 bispecific T-cell engager**, has recently received approval for the treatment of **extensive-stage small cell lung cancer (ES-SCLC)** in patients with disease progression following platinum-based chemotherapy.
- This study aims to assess the safety outcomes related **to cytokine release syndrome (CRS)** and **immune effector cell-associated neurotoxicity syndrome (ICANS)** in real-world setting.







Adverse Event	Grade ≥3 Incidence (%)
AST Elevation	33%
Thrombocytopenia	28%
ALT Elevation	17%

Post First dose Symptoms	Incidence (%)
Fatigue	35%
Nausea and Vomiting	14%
Itching and erythema	14%

RESULTS

- Within our cohort of patients treated with Tarlatamab (n=14), the **median age of patients** was 70 (range: 54-83) years, with 43% females and 64% Caucasian ethnicity**. 93% and 78% of patients received platinum-based chemotherapy and immunotherapy respectively** as previous lines of treatment. 3 patients did not receive immunotherapy due to: autoimmune conditions (n=2) and history of cardiac transplant (n=1).
- The **median lines of treatment** for the cohort was 3 lines (range: 2-4). **35% (n=5) patients** had **previous history of brain metastasis** while **43% (n=6)** patients had **liver metastasis** prior to Tarlatamab initiation.
- We found that **57% of patients had any grade CRS** with **21% patients having CRS on both first and second** doses. Among these, **CRS was mostly grade 1: 28% or grade 2: 21% with 7% patients experiencing grade 3 CRS**. Median time to onset of CRS **was 8 hours (range:1-12)**.
- Characteristic CRS signs/symptoms were **tachycardia (75%), tachypnea (75%), and fever (50%)**. No clear correlation was found between presence of liver metastasis and occurrence of CRS (50% vs 62.5% for patients without liver metastasis).
- For ICANS, **28% of patients had any grade ICANS**, with **all being grade 2 events.** Median onset of ICANS was **9.5 hours** (range: 2-20 hours).
- For other adverse events grade >=3 elevation in **ALT (17%) and AST (33%) elevation, and thrombocytopenia (28%)** were commonly seen. There was no grade 3 anemia, neutropenia or pyrexia. Patient **reported symptoms post first dose** were more commonly**: fatigue (35%), nausea and vomiting (14%).**
- **Median length of hospitalization** was **25.5 hours (range:19-288)** with time between infusion completion and hospital admission being **3 hours 5 minutes (0.5 hours to 9 hours)**. No patients had CRS reported for C1D15 infusion indicating safe infusion in the outpatient setting.

METHODS

- A **retrospective analysis** was conducted on patients who received Tarlatamab for treatment of ES-SCLC from May-November 2024 at **UAB and Infirmary health system.**
- Data variables abstracted included age, sex, and gender, line of treatment and sites of metastasis. Adverse event data focused on the incidence and severity of CRS and ICANS, as well as other treatment-related side effects graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

CONCLUSION

- This real-world study provides valuable insights into the safety of Tarlatamab in ES-SCLC. **The incidence of CRS and ICANS is higher in the real-world setting**, compared to the pivotal clinical trial.
- Future studies should **investigate interventions to reduce CRS/ICANS incidence** and risk factors to improve prediction of toxicity.

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N=14

Median lines of therapy: 3

C1D1 and D15
7% G3 CRS
28% G2 ICANS

PP-01.41: Real-World Intracranial and Extracranial Efficacy Plus Safety Analysis of Tarlatamab in Patients with Extensive-Stage Small Cell Lung Cancer

Mitchell Parma, MD[1]; Eric K Singhi, MD[2]; Kaiwen Wang, PharmD[2]; Melvin Rivera, PharmD[2]; Luisa Solis Soto, MD[3]; Wei-lien Wang, MD[3]; Mehmet Altan, MD[2]; Maria Franco Vega, MD[4]; Alexa Halliday, BA[2]; Joshua Jacome, MPAS, PA-C[2]; Jianjun Zhang, MD, PhD[2]; Xiuning Le, MD, PhD[2]; Jenny Pozadzides, MD[2]; Janet Tu, MD[2]; Celyne Bueno Hume, MD[2]; George Blumenschein, MD[2]; Ferdinandos Skoulidis, MD, PhD[2]; Tina Cascone, MD, PhD[2]; Frank Fossella, MD[2]; Marcelo Vailati Negrao, MD[2]; Natalie Vokes, MD[2]; Don Gibbons, MD, PhD[2]; Haniel Araujo, MD[2]; Anne Tsao, MD[2]; John Heymach, MD[2], PhD; Lauren Byers, MD[2]; Carl M Gay, MD, PhD[2]; Bingnan Zhang, MD[2]

[1]Division of Cancer Medicine, [2]Department of Thoracic/Head & Neck Medical Oncology, [3]Departments of Pathology and Translational Molecular Pathology, [4]Department of Hospital Medicine, University of Texas MD Anderson Cancer Center, Houston, TX.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Background

- Tarlatamab, a bispecific T cell engager (BiTE) therapy targeting Delta-Like Ligand 3 (DLL3), received FDA approval in May 2024 for relapsed extensive stage small cell lung cancer (ES-SCLC).
- Given its unique mechanism of action as a BiTE therapy, unique toxicities of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are expected.
- To mitigate the risk of toxicity, an inpatient step-up dosing schedule is required for cycle 1, day 1 (C1D1) and day 8 (C1D8) (Figure 3), which has limited its rapid adoption, particularly in community practice.
- We report the real-world case series of safety and efficacy data for first cohort of patients treated with standard of care tarlatamab at MD Anderson Cancer Center, with recommended management of CRS and ICANS by MDA CARTOX program.

A

CRS	Criteria	General	Tocilizumab	Steroids
Grade 1	Φεϖερ(□38°C) only	Manage as neutropenic fever Telemetry/pulse ox	1 dose only if fever persists >24 hr	-
Grade 2	Fever + hypotension (IV fluids only) αιδ/ορ ηψποξια(□6Λ/μιν NX)	Manage as neutropenic fever IV fluids / O2	1 dose (can be given Q8hr for 3 doses if not improving) Max 4 doses	▪ Add DEX 4-10mg IV for one time with the second dose of toci ▪ Ιφ νο ιμπροϖεμεντ, ΔΕΞ 10μγ Θ6ηρ(ταπερ when G1 or less) ▪ Consider anakinra if ongoing CRS 2-4 CRS αφτερ6 ηουρσ οφ στεροιδσ
Grade 3	Fever + hypotension (1 vasopressor*) αιδ/ορ ηψποξια(>6Λ/μιν ηιγη low NC, facemask, non-rebreather mask)	As above + ICU transfer ECHO	Toci as G2	▪ ΔΕΞ 10μγ Θ6ηρ (taper when G1 or less) ▪ Worsening BP/pulmonary status on DEX 10mg – ινχρεασε 20μγ Θ6ηρ ▪ Consider anakinra if ongoing CRS 2-4 CRS αφτερ6 ηουρσ οφ στεροιδσ
Grade 4	Fever + hypotension (multiple vasopressor*) and/or hypoxia (CPAP, BiPAP, intubation)	As above + ICU transfer ECHO	Toci as G2	▪ Solumedrol 1gm/day in divided doses for 3 days and then rapid taper ▪ Consider anakinra if ongoing CRS 2-4 CRS αφτερ6 ηουρσ οφ στεροιδσ ▪ If no improvement in 24 hr or worsening, additional therapies

B

ICE scores for ICAN assessment
10: no impairment
7-9, grade 1 ICANS
3-6, grade 2 ICANS
0-2, grade 3 ICANS*

Parameter	Score (Points)
Orientation: year, month, city, hospital	4
Naming: ability to name 3 objects (eg, point to clock, pen, button)	3
Following commands: ability to follow simple commands (eg, "show me 2 fingers" or "close your eyes and stick out your tongue")	1
Writing: ability to write a standard sentence (eg, "our national bird is the bald eagle")	1
Attention: ability to count backwards from 100 by 10	1

* A patient with an ICE score of 0 may be classified as having Grade 3 ICANS if the patient is awake with global aphasia or may be classified as having Grade 4 ICANS if the patient is unarousable

ICANS	Criteria	General	Steroids
Grade 1	ICE score 7-9 Awakens spontaneously	MRI/CT brain Neuro consult EEG Χονσιδερ ΛΠ	-
Grade 2	ICE score 3-6 Awakens to voice	As above	ΔΕΞ 10μγ Θ6ηρ (taper when G1 or less)
Grade 3*	ICE Score 0-2 Awakens only to tactile stimuli Any seizure Focal edema on neuroimaging	As above + ICU transfer	ΔΕΞ 10μγ Θ6ηρ (taper when G1 or less) Consider IT chemo
Grade 4*	ICE Score 0 Unarousable or requires vigorous/ repetitive stimuli to arouse; Coma Λιφε-τηρεατ πρoλονγεδ (□5 μιν) seizures Hemiparesis/paraparesis Diffuse edema on neuroimaging; papilledema Decerebrate/decorticate posturing	As above + ICU transfer	Solumedrol 1gm/day in divided doses for 3 days and then rapid taper; If no improvement in 24 hr or worsening, additional therapies Consider IT chemo

Smart phone app available free on both App Store (iPhone) and Google Play (Android)

Figure 1: MD Anderson's CARTOX reference tables for CRS (A) and ICANS (B) grading and management,, based on ASTCT consensus grading guidelines. Reference: Neelapu et al. *Nat Rev Clin Oncol*, Jan 2018; Lee et al. *Biol Blood Marrow Transplant*, 2019.

Methods

- We queried the MD Anderson Lung Cancer IRB-approved GEMINI database for patients treated with tarlatamab and retrospectively collected demographic, clinical, and outcome data.
- From 7/1/2024-1/15/2025, a total of 39 patients received tarlatamab.
- 8 patients were excluded from analysis either due to diagnosis of extrapulmonary small cell cancer or rapid clinical deterioration due to disease progression around the time of the first tarlatamab infusion.
- The final cohort consisted of 31 patients.

Results

Demographic and Baseline Clinical Characteristics (N=31)	
Average Age (range) – yr	66 (42 – 83)
Sex – no. (%)	
Male	12 (39)
Female	19 (61)
Race – no. (%)	
White	20 (64)
Asian	8 (26)
Black	3 (10)
Smoking Status – no. (%)	
Former Smoker	17 (55)
Current Smoker	8 (26)
Never Smoker	6 (19)
Median ECOG	**1**
Patient Location – no. (%)	
Houston, TX	4 (13)
Texas (outside Houston)	17 (77)
USA (outside Texas)	9 (29)
International	1 (3)
Initial Stage – no. (%)	
ES-SCLC	18 (58)
LS-SCLC	9 (29)
EGFR NSCLC transformed*	**4 (13)**
Median lines of therapy prior to Tarlatamab (range)	**2 (1-6)**
Duration of 1st line platinum-based therapy response – no. (%)	
<90 days	12 (39)
90-180 days	9 (29)
>180 days	10 (32)
Presence of Brain metastases (BM) prior to Tarlatamab – no. (%)	
No BM	9 (29)
Treated BM	10 (32)
Untreated BM	12 (39)
*3 EGFR 19 deletion, 1 EGFR L858R mutation	

Figure 2: Demographic and baseline clinical characteristics.

31 Patients C1D1

28 Patients C1D8

25 Patients C1D15*

At the data cut-off, 17 had repeat systemic scans and 18 had repeat brain MRIs

Figure 3: General flow and timestamps of our cohort at time of data collection: *For C1D15, 20 patients received therapy outpatient, while 5 patient received it inpatient. 2 patients had also transitioned their care to an outside institution.

Safety Data from C1D1 and C1D8 of Tarlatamab		
Adverse Event	**Hospitalization for C1D1 of Tarlatamab 1 mg IV (N=31)**	**Hospitalization for C1D8 of Tarlatamab 10 mg IV (N=28)**
Median Hospitalization stay – days	3	3
Cytokine-release syndrome – no. (%)		
Overall	12 (39)	11 (39)
Grade 3 or more	1 (3)	1 (4)
Median time from start of Tarlatamab infusion to first sign of CRS - hours	9	24
Tocilizumab Administration	10 (32)	4 (14)
ICANS – no. (%)		
Overall	8 (26)	4 (14)
Grade 3 or more	4 (13)	0 (0)
Development of seizures	0 (0)	0 (0)
Adverse event leading to ICU stay – no. (%)		
Overall	4 (13)	1 (4)
Median duration – days	2	6
Requirement of pressors	0 (0)	1 (4)
Requirement of oxygen supplementation beyond nasal cannula	0 (0)	1 (4)

Figure 4: Safety data from C1D1 and C1D8 of tarlatamab

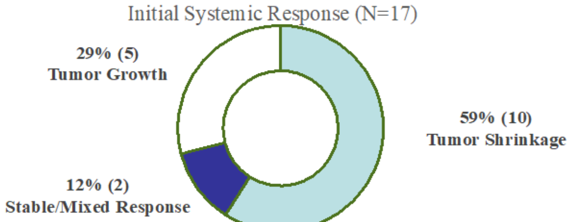


Figure 5: Initial systemic response rates based on first reimaging PET/CT scans following treatment

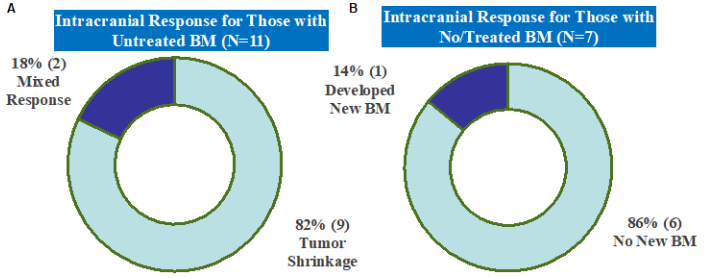


Figure 6: Initial intracranial response based on repeat brain MRI following tarlatamab: A. For patients who had radiographic evidence of untreated BM prior to treatment. **B.** for patients who either had no BM prior to treatment, or who had treated BM prior to tarlatamab.

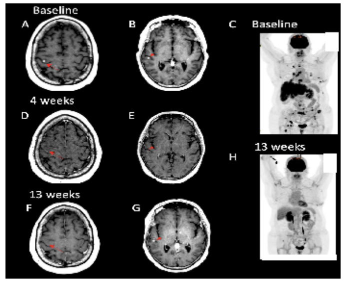


Figure 7: Radiographic example of a patient who achieved both systemic and intracranial tumor control.

Patient 1
- Systemic tumor growth on initial restaging PET/CT scan
- Having had treated BM prior to tarlatamab, initial repeat brain MRI showed new BM

Patient 2
- Achieved systemic tumor shrinkage on initial restaging PET/CT scan
- Having untreated BM prior to treatment, initial repeat brain MRI showed mixed response

Patient 3
- Developed systemic tumor growth on initial restaging PET/CT scan
- No repeat brain MRI done.

Patient 4
- Expired from infection related complication prior to repeat imaging.

Figure 8: Outcomes in patients with EGFR NSCLC transformed to SCLC.

Conclusion

- Preliminary data from this real-world cohort of tarlatamab show promising efficacy especially in patients with untreated intracranial metastases.
- We observed higher rates of CRS and ICANS in our cohort of patients compared to those reported in the clinical trials.
- Additional data collection and analyses are ongoing at this time.

Presenter Information

Mitchell Parma, MD
Hematology/Oncology fellow, University of Texas MD Anderson Cancer Center
Email: maparma@mdanderson.org

N=31

Median lines of therapy =2

Safety C1D1 and C1D8
>/=G3 CRS: 3-4%
>/=G3 ICANS 13% with no seizures

Efficacy on 1st restaging (tumor shrinkage)

Systemic response =59% (10/17)

Intracranial response in untreated brain mets=82% (9/11)

MCC data

- 40 patients with SCLC treated with at least one dose of tarlatamab during cycle 1(C1) at MCC (May-February 2024)
- Median age - 66.5years (range: 49-81)
- Median prior lines: 70% </=2 lines
- 87% with ECOG PS 0-1
- At the time of tarlatamab initiation, >25% had worsening CNS disease (17.5% at baseline), and >45% had new/worsening liver metastases (32% at baseline).

Unpublished data.
Under review. Clinical Lung Cancer Oct 2025

Characteristics of Ineligible Patients by DeLLphi-301 trial Exclusion Criteria (N=40)

DeLLphi-301 trial's exclusion criteria at cycle 1 day 1 of tarlatamab	Patients (N=40) n (%)
Untreated or symptomatic brain metastases or leptomeningeal disease	11 (27.5)
Inadequate organ function (renal, cardiac, hepatic)	
GFR ≤ 30 ml/min	1 (2.5)
AST, ALT, or ALP >3x ULN or >5x ULN for patient with liver involvement	2 (5)
Total bili >1.5x ULN or >2x ULN for patient with liver involvement	2 (5)
ECOG performance status ≥2	5 (12.5)
Cytopenia	
Platelet count < 90	2 (5)
Hemoglobin < 9 g/dL	4 (10)
Active malignancy within the last 2 years of C1D1	6 (15)
Transformation from non-small cell lung cancer	3 (7.5)
Mixed histology	8 (20)

Introduction of prophylactic tocilizumab

- 3 patients (~11%) experienced severe adverse events related to CRS/ICANS leading to death or transition to hospice post C1D1 hospitalization (1 G4 CRS with G3 ICANS, 1 G4 CRS, 1 G4 ICANS with G3 CRS).
- Based on this observation prophylactic tocilizumab prior to C1D1 was implemented for high-risk features identified in the limited patient cohort with an ability to repeat dosing with subsequent cycles based on treating physicians' discretion.

Introduction of prophylactic tocilizumab

Prophylactic tocilizumab (8 mg/kg) was implemented at our institution for patients considered to have a high-risk for AEs based on clinical and laboratory factors.

Clinical risk factors

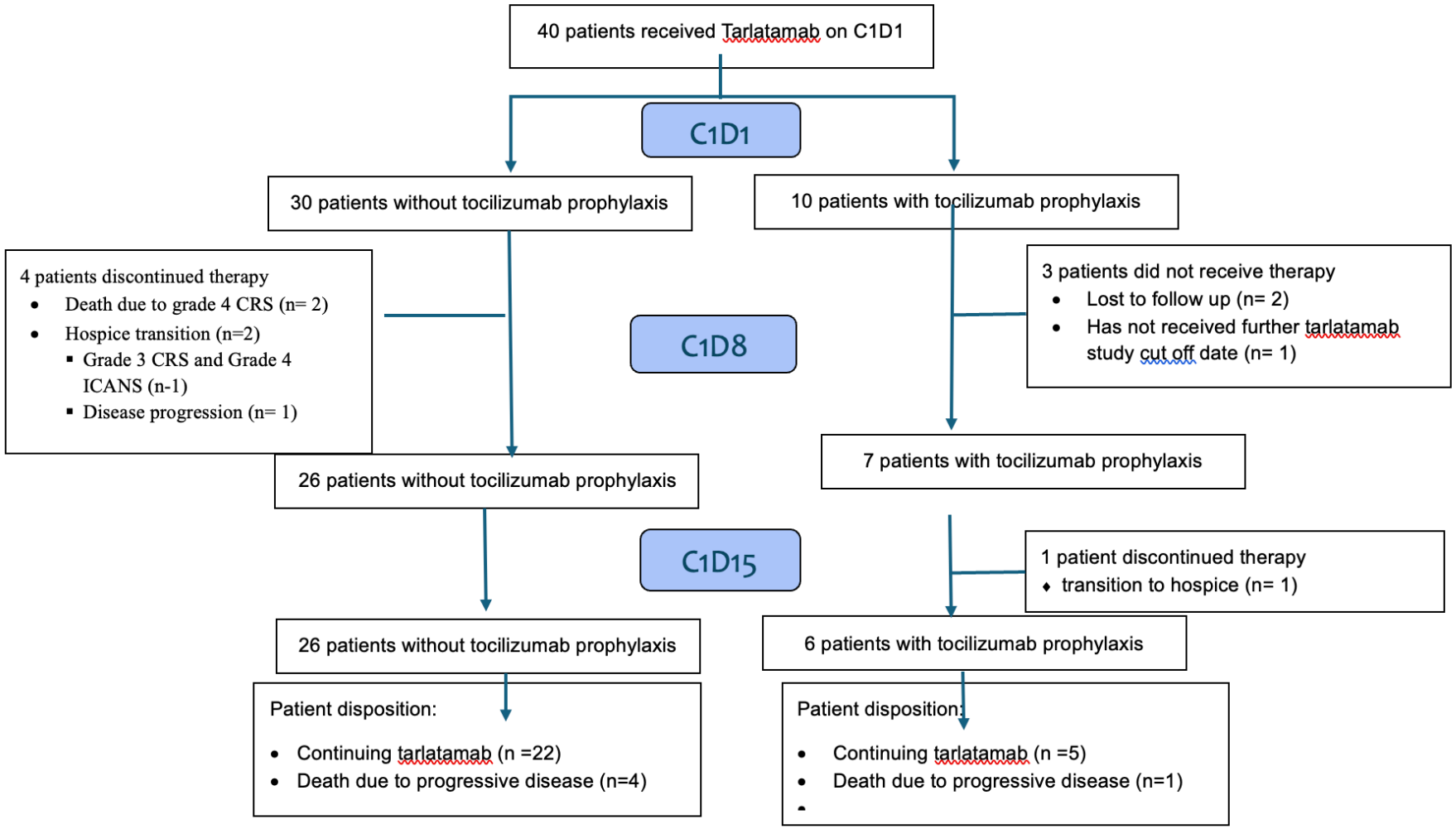
- advanced age (>75 years),
- multiple comorbidities,
- primary tumor size ≥7 cm,
- diffuse or innumerable hepatic metastases, or multiple coalescing hepatic lesions (treating physician interpretation of radiology).

Laboratory risk factors

- elevated baseline inflammatory markers: LDH ≥500 U/L, CRP ≥4 mg/dL, ferritin ≥400 ng/mL, and uric acid ≥8.4 mg/dL.

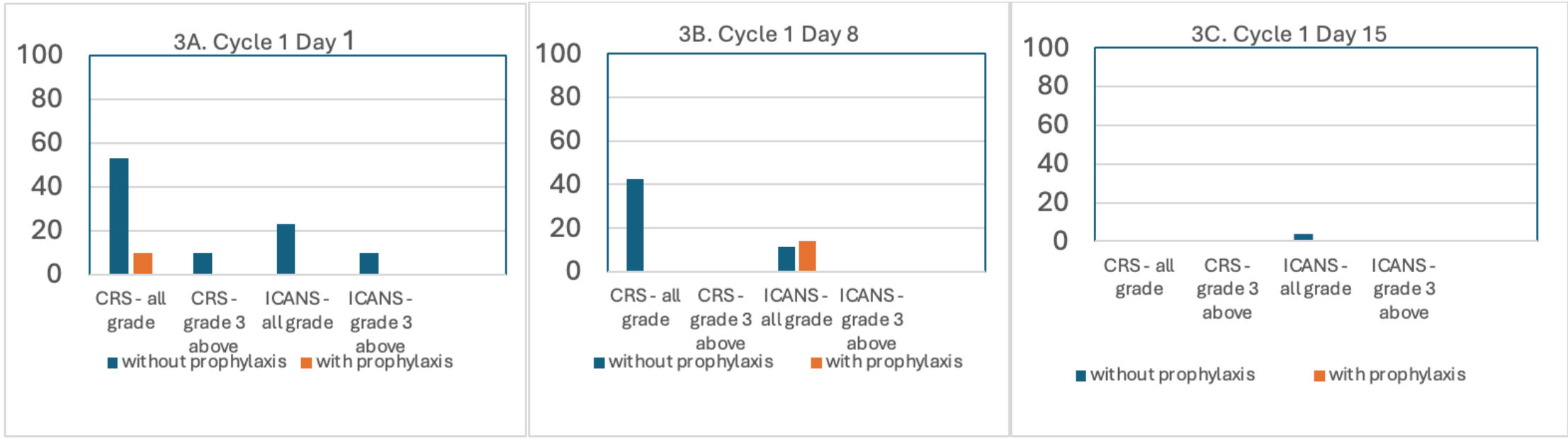
Repeat dosing in subsequent cycles was left to the discretion of the treating physician.

Figure 2. Patient Journey through Cycle 1 of tarlatamab



Safety

Figure 3. Incidence of CRS and ICANS with cycle 1 of tarlatamab



CRS: cytokine release syndrome; ICANS: immune effector cell-associated neurotoxicity syndrome

w/o toci N=30
C1D1-53% all grade CRS, 10% >/=G3, 23% any grade ICANs, 10% >/=G3
C1D8 42% all grade CRS, no G3, 11% ICANs all </=G2
w toci N=10: 1 patient with G2 CRS in C1D1, 1 patient with ICANs C1D8

Preliminary response data

Patients who did not receive prophylactic tocilizumab (Evaluable patients, N=23),

11 (47.8%) achieved a disease response (physician assessed best response)

12 (52.1%) experienced disease progression.

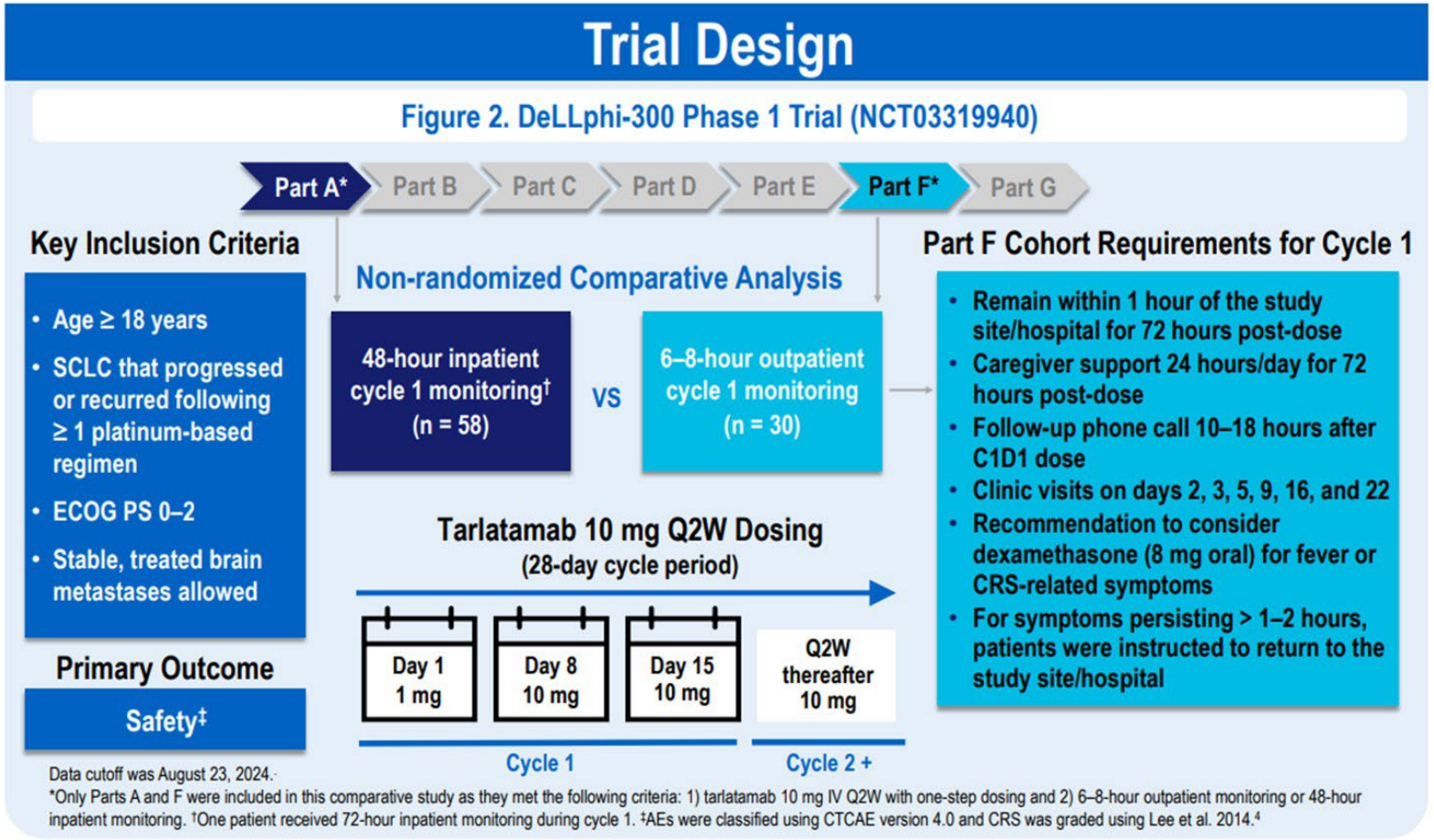
Patients in the prophylactic tocilizumab group (Evaluable , N=6)

3 patients (50%) achieved a disease response

3 patients (50%) experienced disease progression.

Can Tarlatamab Be Given as an Outpatient Setting?

Phase I DeLLphi-300 **Part F—Out-patient "Pilot"**



Chiang et al ESMO-IO 2024

Can Tarlatamab Be Given as an Outpatient Setting?

Tarlatamab: Case Study for Out-Patient Management

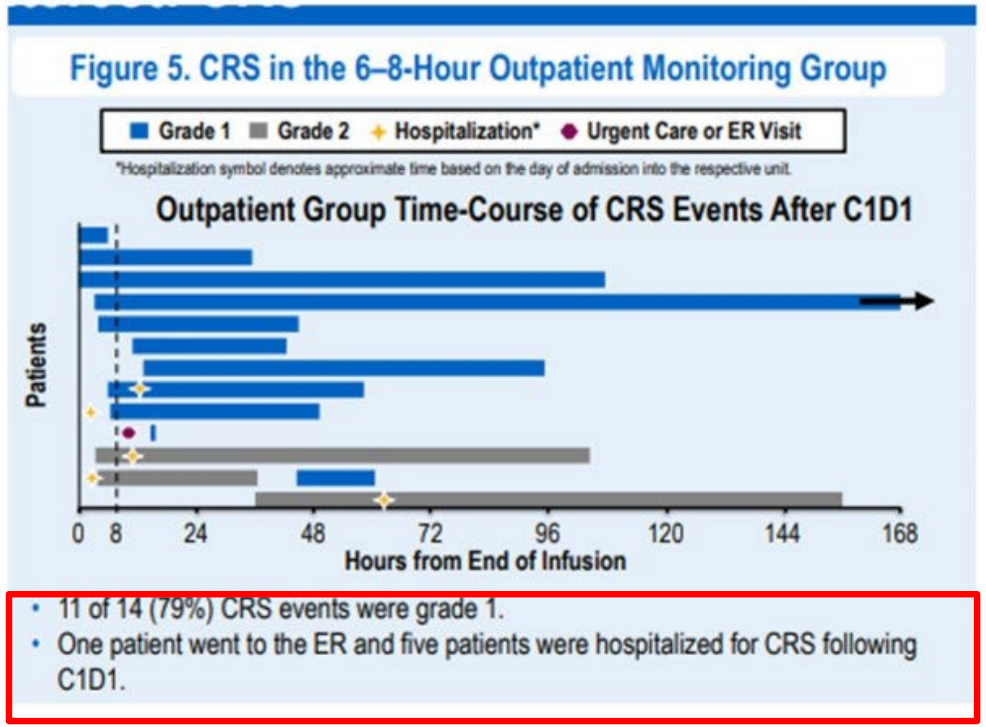
TRAEs Occurring in ≥25% of Patients (All Cycles)

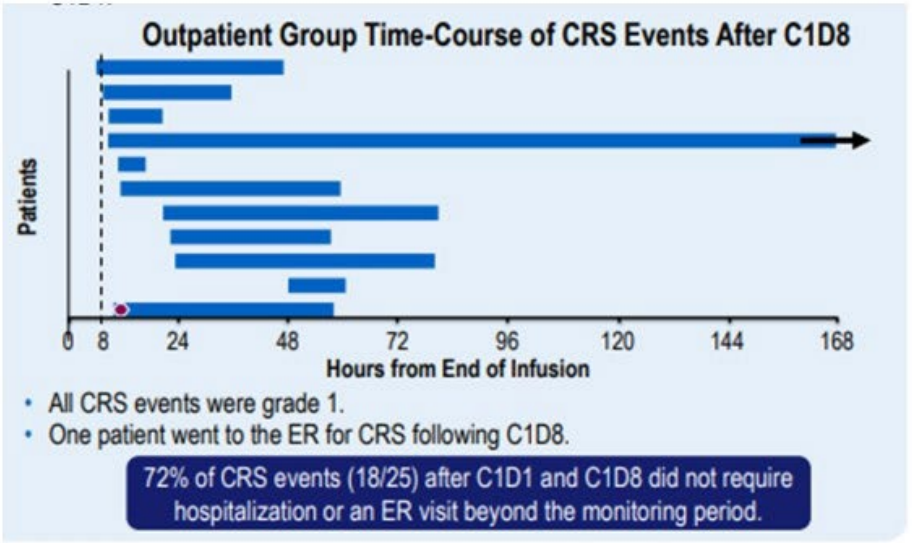
Preferred Term, n(%)	6-8 Hr OUTpatient Monitoring(n=30)	48 Hr INpatient Monitoring(n=58)
CRS	18 (60)	36 (62)
Dysgeusia	14 (47)	25 (43)
Nausea	11 (37)	10 (17)
Asthenia	10 (33)	9 (16)
Decreased appetite	9 (30)	12 (21)
Pyrexia	8 (27)	18 (31)
Fatigue	7 (23)	17 (29)

adapted from Chiang et al ESMO-IO 2024

Can Tarlatamab Be Given as an Outpatient Setting?

72% of CRS events after C1D1 and C1D8 did not even require hospitalization or ER visit





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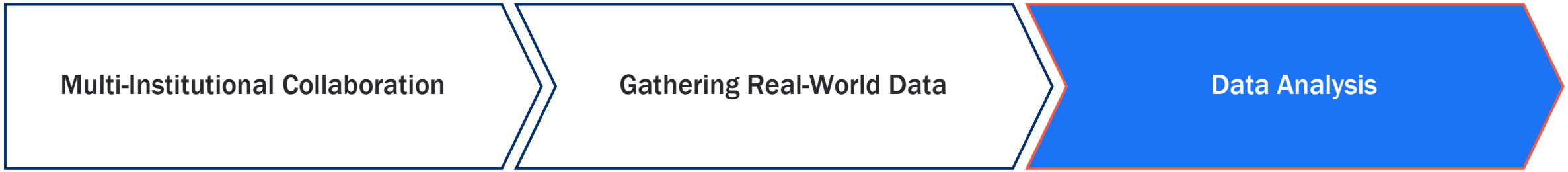
Bridging the gap

Bridging the Gap

- **Hub-and-spoke models:** Initiation at academic centers with transition to community sites for maintenance
- **Remote monitoring:** Telehealth check-ins, hospital at home programs
- **Standardized protocols:** Algorithms/checklists for CRS/ICANS detection
- **Education and outreach:** Community-facing CME programs, toolkits for toxicity management
- **Partnership models:** Case conferencing.

ONWARD –SCLC

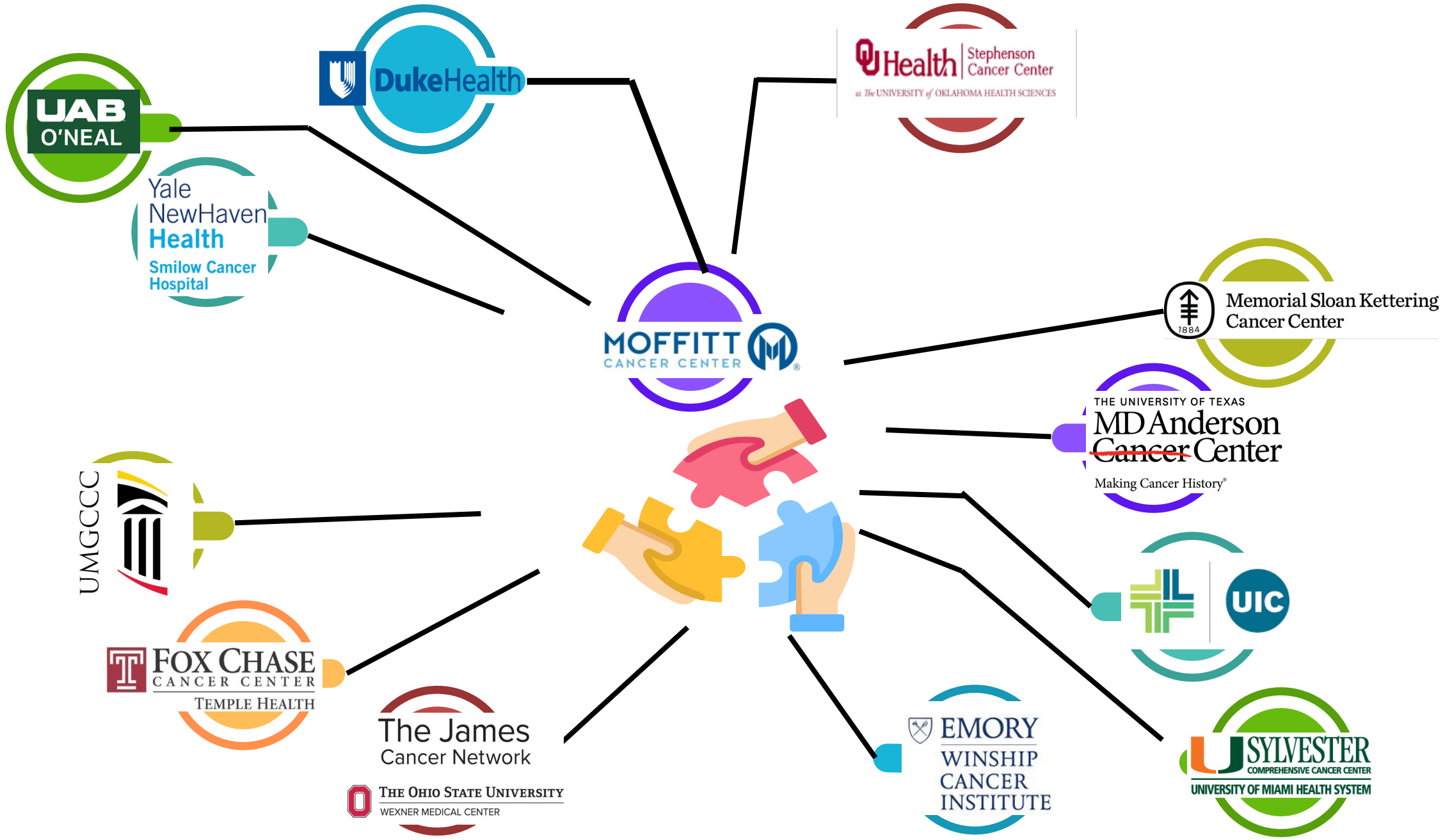
Observational Network for Advancing Real-World Data in SCLC



The ONWARD consortium brings together a diverse group of leading academic and research institutions to collaborate on this initiative.

The consortium will collect data from electronic medical record .

The consortium will analyze the gathered real-world data to gain insights and advance the understanding of small cell lung cancer.


UAB O'NEAL
DukeHealth
OU Health Stephenson Cancer Center
at The University of Oklahoma Health Sciences
Yale NewHaven Health Smilow Cancer Hospital
MOFFITT CANCER CENTER
1884
Memorial Sloan Kettering Cancer Center
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®
UMGCCC
UIC
FOX CHASE CANCER CENTER
TEMPLE HEALTH
The James Cancer Network
THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER
EMORY WINSHIP CANCER INSTITUTE
SYLVESTER COMPREHENSIVE CANCER CENTER
UNIVERSITY OF MIAMI HEALTH SYSTEM

ONWARD –SCLC : Real world questions

Real world questions

- Efficacy in mixed / transformed lung cancer histologies
- Efficacy in large cell neuroendocrine tumors
- Efficacy in extra pulmonary SCLC
- Larger data on intracranial efficacy
- CRS/ ICANS mitigation strategies

Take Home Points

⚑ Mechanism of Action

- T-cell engagers (TCEs) link CD3 on T cells to tumor antigens, triggering immune synapse and tumor cell killing

⚠ Toxicity Profile

- CRS and ICANS are common, often within 24–48h post-dose
- Requires early recognition and prompt management (e.g., tocilizumab, steroids)

⏱ Importance of Early Detection

- Monitor for subtle symptoms: fever, hypotension, confusion
- Train frontline staff for rapid triage and escalation

🚧 Operational Readiness

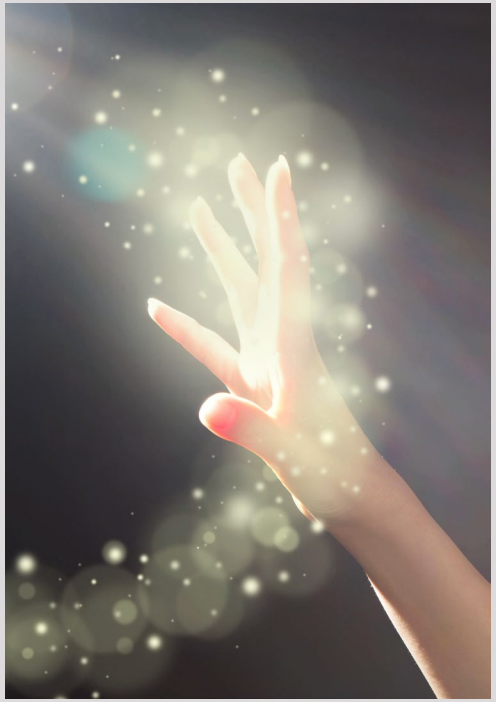
- Needs step-up dosing protocols, infusion center coordination, and emergency preparedness
- Outpatient transition depends on structured follow-up

🏘 Bridging Practice Gaps

- Community sites may lack experience with TCEs
- Hub-and-spoke models, shared protocols, and telehealth support can improve access

🌍 Pipeline & Approvals

- Many TCEs in development for solid tumors (HER2, EGFR, PSMA, DLL3, etc.)
- FDA-approved: **Tebentafusp** (uveal melanoma), **Tarlatamab** (SCLC)



Thank you !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