TRIO HEALTH

REAL-WORLD EVIDENCE STUDY • RRMM

Building a relapsed/refractory myeloma cohort from EHR data, and testing cilta-cel against a matched real-world control

A Trio Health study of relapsed or refractory myeloma across two data networks, with a 1,028 patient cilta-cel arm benchmarked against a matched comparator and the CARTITUDE-4 trial.

Lambda + Omega network · Notes confirmed relapsed or refractory, approximately 17,500 · Report date 23 July 2026

BACKGROUND & RATIONALE • 01

Does the trial evidence hold up **in routine practice?**

Cilta-cel is a BCMA-directed CAR-T therapy for RRMM, approved on the CARTITUDE-1 and CARTITUDE-4 trials. Real-world data test whether those results hold in a broader, less-selected population, and add the operational texture (bridging, CRS and ICANS management, end-of-life care) that trials report only in aggregate.

HOW TO READ THIS

Four terms that carry the rest of the deck

This study uses a small amount of specialist vocabulary. Everything else follows from these four ideas.

Relapsed / refractory myeloma (RRMM)

The cancer has come back after responding to treatment, or has stopped responding altogether. A relapse code exists but only about half of these patients carry it, and refractory has no code at all.

The comparator group

Patients with the same disease stage, age, sex and treatment era who started a different therapy instead. They stand in for the control group a clinical trial would randomise.

Cilta-cel (Carvykti)

A CAR-T cell therapy. The patient's own immune cells are removed, re-engineered to recognise myeloma, and given back as a single infusion at a specialist centre.

Time to next treatment (TTNT)

How long a patient goes before needing another myeloma therapy. Longer is better, it means the disease stayed under control. It is the real-world stand-in for the trial's progression-free survival.

THE BENCHMARK

Two pivotal trials anchor the comparison

Together they bracket the real-world cohort: CARTITUDE-4 in earlier-line, lenalidomide-refractory disease, and CARTITUDE-1 in heavily pretreated, triple-class-exposed patients.

CARTITUDE-4

NCT04181827

Phase 3, cilta-cel vs standard of care (PVd or DPd)

POPULATION

Lenalidomide-refractory, 1 to 3 prior lines

KEY RESULTS

ORR **84.6%**, CR or better **73.1%**

Median PFS not reached vs 11.8 months. 30-month OS 76.4%.

CRS 76% (1% grade 3+). ICANS 5%, broad neurotoxicity 21%.

CARTITUDE-1

Phase 1b/2

Single-arm registrational study

POPULATION

Heavily pretreated, 3 or more prior lines, triple-class exposed

KEY RESULTS

ORR **~98%**, sCR **~83%**

2-year PFS ~61%. 2-year OS ~74%.

CRS 95% (4% grade 3+).

> *The real-world cohort spans both trial populations, providing a natural bridge between the earlier-line randomized and the heavily-pretreated single-arm settings.*

A trial-replication framework, applied at scale

THE METHOD · 4 PHASES · LAMBDA + OMEGA, COMBINED

Every patient follows the same path, from finding the cohort through to benchmarking, so the real-world figures line up cleanly against the trial.

1

FUNNEL

Find the patients

Start from every myeloma patient, narrow to those on treatment, then to those whose disease has relapsed or stopped responding.

2

COVERAGE

Check it is written down

Before extracting anything, measure how often each fact actually appears in the record. No point extracting what was never documented.

3

EXTRACT

11 variables, AI plus QC

Read the notes and write each finding to a defined field, with the source sentence kept alongside it.

4

ANALYZE

Compare and benchmark

Build a matched comparison group, measure outcomes in both, and set the results against the CARTITUDE trials.

Lambda and Omega are reported separately or summed without cross-asset de-duplication, never blended.

EXTRACTION • VARIABLES DEFINED BEFORE EXTRACTION

What we extract, how it is defined, and where it comes from

Structured, anchored on a code Note-extracted, AI plus clinical QC

VARIABLE	DEFINITION	SOURCE
Multiple myeloma diagnosis	MM diagnosis anchoring cohort entry	**Structured ICD-10 C90.0x**
Anti-myeloma therapy exposure	Orders, administrations and pharmacy fills, unioned	**Structured, all medication sources**
Relapsed / refractory status	Relapse after response, or progression on therapy	**Note-extracted, drug-agnostic**
Prior lines & lenalidomide-refractory	Regimen history and refractory status	**Structured Rx + note-confirmed**
Measurable disease (IMWG)	M-protein, free light chain, or plasmacytoma	**Note-extracted**
Bridging therapy	Therapy between apheresis and infusion	**Note-extracted**
Response (IMWG)	sCR, CR, VGPR, PR, SD, or PD	**Note-extracted**AI + QC
MRD status	MRD-negative, with threshold when stated	**Note-extracted**flow / NGS
CRS & neurotoxicity	ASTCT grade, type, and management	**Note-extracted**AI + QC

Codes shown are the structured anchors used for cohort entry. The CAR-T-specific variables, bridging, MRD, CRS and neurotoxicity, apply to the cilta-cel arm only; the cohort and comparator work uses 11.

PHASE 1 • COHORT FUNNEL

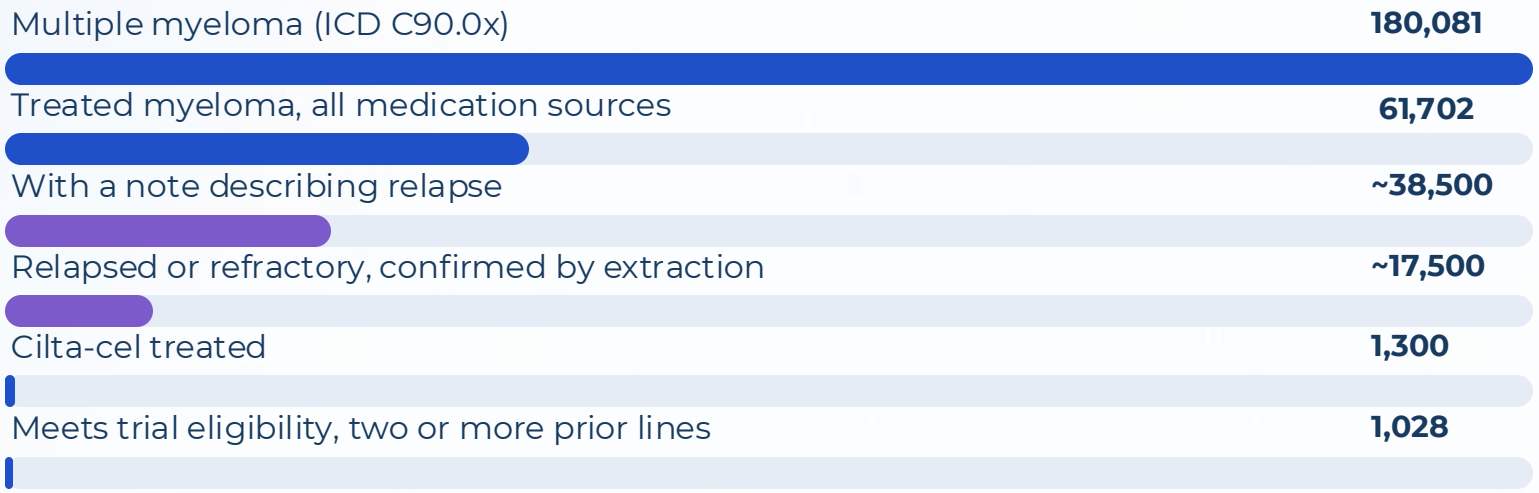
Finding the patients the relapse code misses

~17,500

Relapsed or refractory patients confirmed by reading clinical notes. Lambda 9,848, Omega 7,615.

> Relapsed or refractory means the disease came back, or stopped responding. A relapse code exists but only about half of these patients carry it, and refractory has no code at all.

COHORT FUNNEL · COUNTS AND SAMPLE BASED ESTIMATES



Blue rows are exact counts from structured records. Purple rows are estimated by extrapolating the 2,000 patient sample; the confirmed relapsed figure carries a 95% confidence interval of 15,800 to 19,200. Eligibility here is the two or more prior lines criterion used for the matched comparison.

- Start from every patient carrying a myeloma diagnosis code
- Keep those with any anti myeloma therapy: prescriptions, clinic administrations, pharmacy fills
- Funnel counts are exact; the notes confirmed figure is estimated from a 2,000 patient sample
- Whole population, no matching at this stage

COHORT IDENTIFICATION • RELAPSED / REFRACTORY STATUS FROM NOTES

The system decides, and it is allowed to say no

Every note containing relapse language is read in full and classified. This is not a keyword search: the model must make a call, and it can rule a patient out. Basis for the call across all notes, clinical 1,071, biochemical 286, imaging 90.

WHAT NOTE EXTRACTION RETURNED • COMBINED SAMPLE, N = 2,000 PATIENTS

> Positives are 45% of every note that matched, in both networks independently: 45.0% Lambda, 45.8% Omega. Two separate datasets agreeing this closely is what gives confidence in the classifier.

EXAMPLE NOTE EVIDENCE • CONFIRMED RELAPSED / REFRACTORY

> "Obtained complete hematologic remission based on lack of monoclonal protein. However has had hematologic and radiographic progressive disease."

> "...progression of the myeloma on Revlimid and that he should switch to Velcade"

EXAMPLE NOTE EVIDENCE • CONFIRMED NOT RELAPSED / REFRACTORY

> "Newly diagnosed R-ISS stage III IgA kappa multiple myeloma with good response to induction therapy"

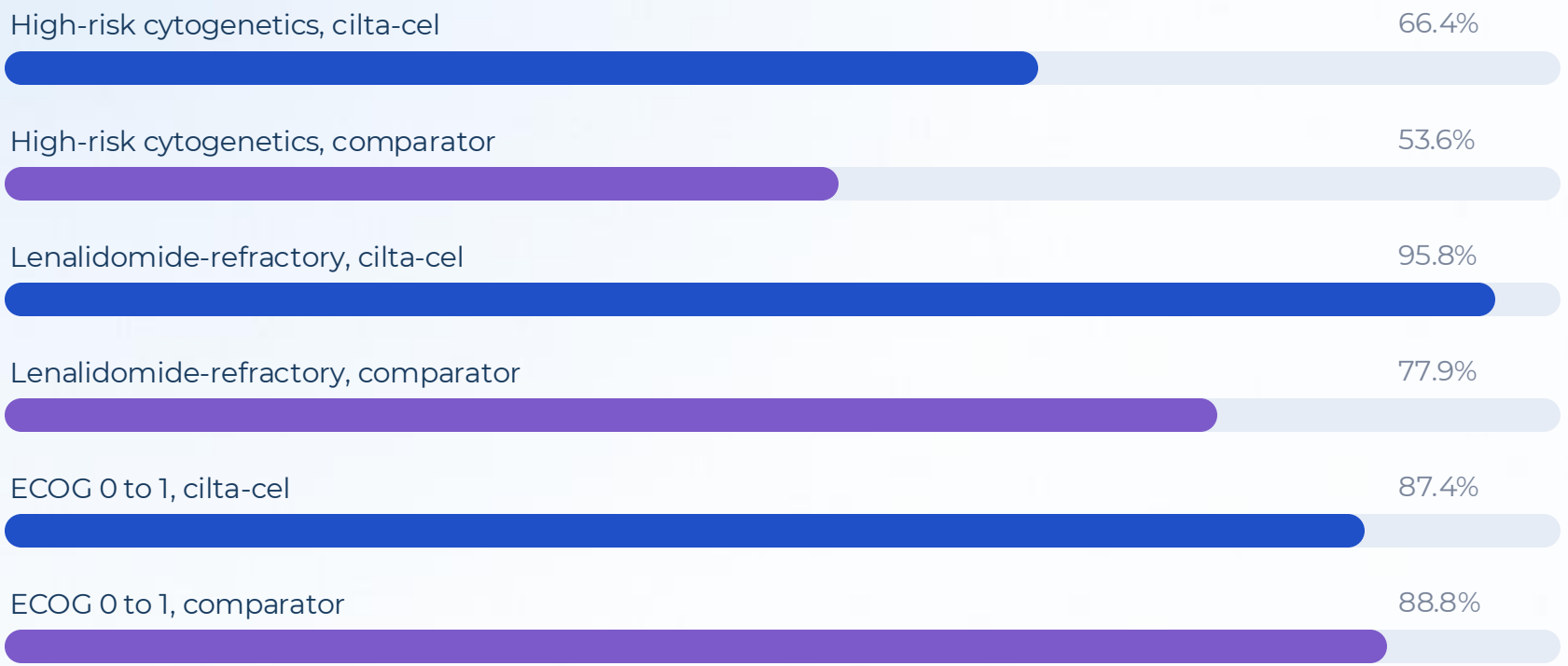
> "...remained in remission on maintenance daratumumab and lenalidomide therapy, with no clinical evidence of disease progression"

BASELINE • CILTA-CEL ARM vs MATCHED COMPARATOR

The treated arm carries more high-risk disease

The two groups are matched on sex, age band, number of prior treatments and calendar era. Cytogenetic risk, whether the myeloma carries high-risk chromosome changes, was deliberately not matched, and it differs.

BASELINE FEATURES • SHARE WITH THE FEATURE, AMONG PATIENTS WHERE IT WAS DOCUMENTED



66%

High-risk cytogenetics, cilta-cel arm

The treated group is the sicker group. That works against cilta-cel in every comparison that follows, so any advantage it shows is achieved despite a harder starting position.

- Matched on: sex, 10 year age band, prior line count, calendar era from 2022
- Not matched on: cytogenetic risk, disease stage, frailty, referral access, payer
- All three features shown are curated from clinical notes
- Coded fields were not used for these values

RESPONSE • FULL CILTA-CEL COHORT • N = 397 EVALUABLE

Deep responses in the treated group

Overall response means the myeloma measurably shrank. Complete response means it became undetectable by standard testing. The matched-comparison subset reached 91.3% and 66.0%, against the comparator's 89.2% and 50.0%.

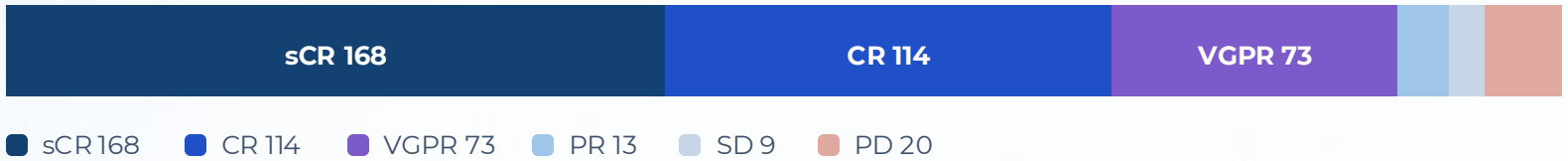
92.7% ORR, PR or better 368 of 397

Full cohort. CARTITUDE-4 cilta arm 84.6%.

71.0% CR or better, sCR plus CR 282 of 397

Full cohort. CARTITUDE-4 73.1%.

RESPONSE DISTRIBUTION • N = 397



487 of the 778 patients with a documented MRD test were MRD-negative, no myeloma detectable even by the most sensitive assay available, the deepest tier of response.

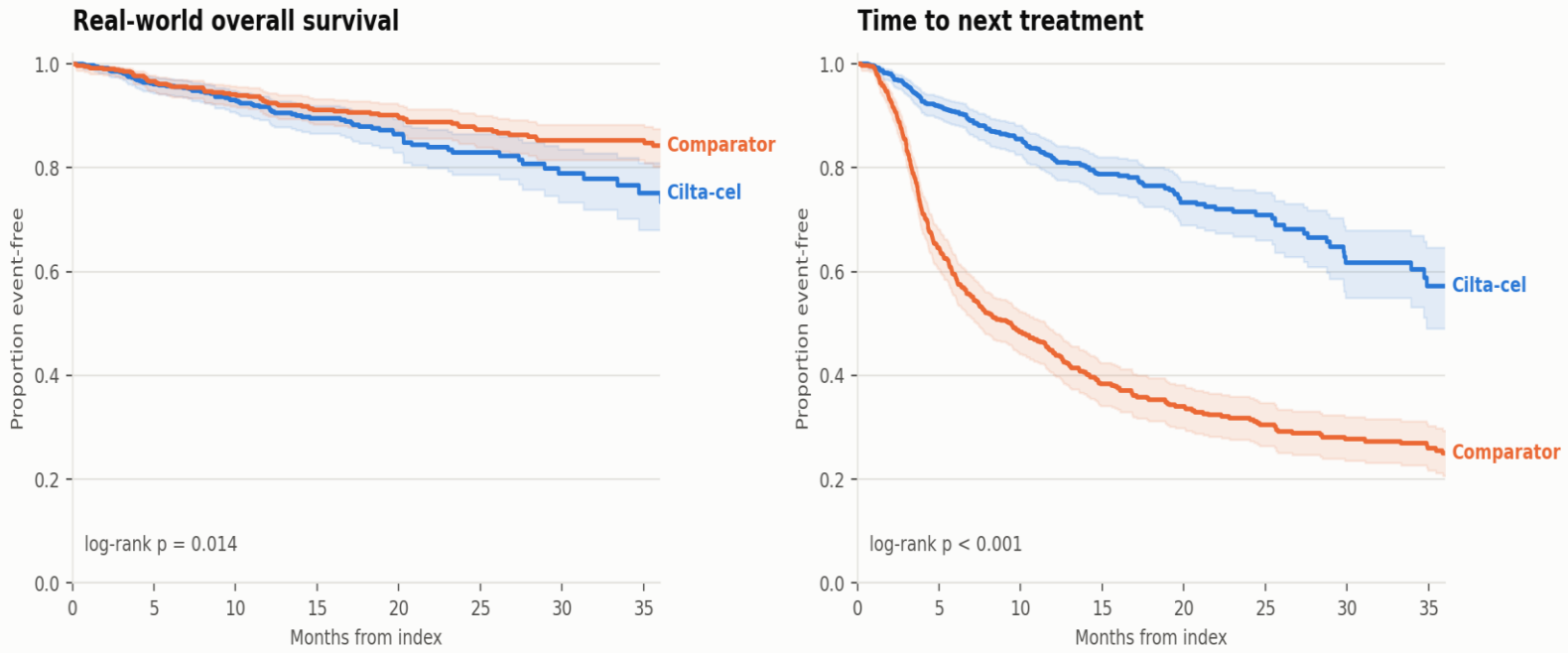
- Response is curated from clinical notes, not central trial assessment
- Denominator is patients with a documented response, about 30% of each arm
- Rates describe the documented subset, not the whole cohort

SURVIVAL • CILTA-CEL vs MATCHED COMPARATOR • LAMBDA

Time to next treatment separates sharply; survival does not

KAPLAN-MEIER ESTIMATES • CILTA-CEL (n = 767) vs COMPARATOR (n = 630)

Cilta-cel vs matched comparator — Lambda, index 2022+



Associational, not causal. Arm B matched on sex x age band x lines proxy x era. Censoring at last activity biases both arms optimistic.

Overall survival

92% at 12 months

83% at 24 months

Therapy-free (TTNT)

82% at 12 months

72% at 24 months

Time to next treatment is how long a patient goes before needing another myeloma therapy: longer means the disease stayed controlled. 38.6 months for cilta-cel against 9.4 for the comparator, versus the trial's not-reached against 11.8.

Overall survival does not separate (83.0% vs 87.9% at 24 months). It is the least mature figure here: few deaths so far, short follow-up, and patients drop out of view when they are treated elsewhere, which flatters both groups.

- Time to next treatment: first drug class absent from the starting regimen, from structured records
- Defined identically in both arms
- Survival uses Lambda structured death records; Omega has none, so survival is Lambda only

DATA AVAILABILITY • WHAT THE RECORD SUPPORTS

The trial's entry criteria are the worst-documented fact

How often each fact can actually be determined from a patient's record, measured on a random 2,000-patient sample in each network independently.

BEST DOCUMENTED

59.3%

measurable disease (IMWG)

43.5%

relapsed / refractory status

Among comparator patients, subsequent therapy reaches 66% in Lambda and 87% in Omega.

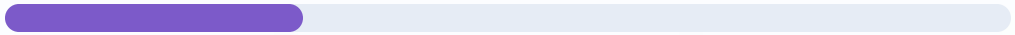
WORST DOCUMENTED

9.3%

prior lines of therapy

2.3%

lenalidomide-refractory status



Both are CARTITUDE-4 entry criteria, the facts a trial would screen on. A study design that requires them would lose most of its eligible patients not because they are ineligible, but because nobody wrote it down.

- Random 2,000 patient sample, every relevant note read
- Measures how often each fact can be determined at all
- This is about documentation, not about the patients' disease
- No matching applies

HEAD-TO-HEAD

How the real-world cohort compares to the trials

The Trio column is the cilta-cel group restricted to patients with two or more prior treatments, so it lines up with who the trials enrolled. Read down it to compare like with like.

	RWE, combined Trio, Lambda + Omega	CARTITUDE-4 Ph 3, cilta arm	CARTITUDE-1 Ph 1b/2
N	**1,028 (arm A)**	208	97
Median prior lines	**3**	2	6
High-risk cytogenetics	**53%**	~60%	~24%
ORR	**91.3%**	84.6%	~98%
CR or better	**66.0%**	73.1%	~83%(sCR)
CRS (any / grade 3+)	**67.5% / 0.8%**	76% / 1%	95% / 4%
Neurotoxicity	**29.6%**	21%(ICANS 5%)	21%(ICANS 17%)
Median OS	**NR**, 24-mo 84%	NR, 30-mo 76.4%	NR, 2-yr 74%
PFS / TTNT	**Median TTNT 38.6 mo**	NRvs 11.8 mo SOC	2-yr PFS 61%

The matched real-world comparator reached a median TTNT of 9.4 months, close to the CARTITUDE-4 standard-of-care arm at 11.8 months, an independently constructed control behaving like the randomised one.

- Real world column restricted to patients with two or more prior treatments
- Trial figures are published results
- Response and safety are curated; survival and time to next treatment are structured

BEYOND THE ENDPOINTS • 02

What the real-world data add**beyond the trials**

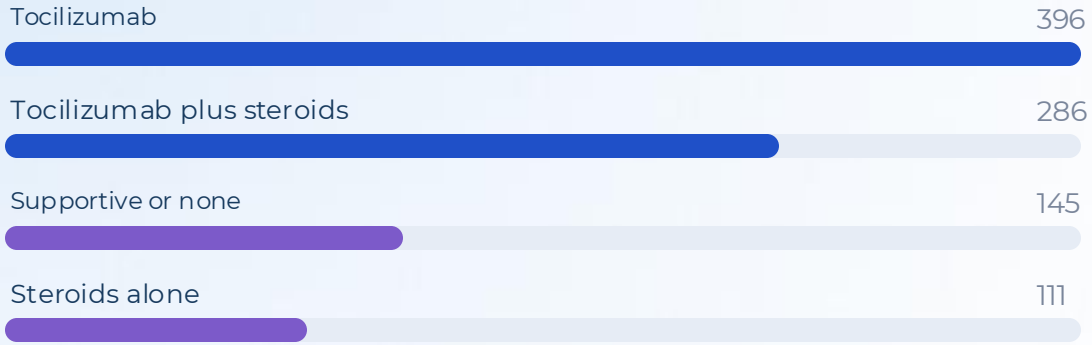
Trials report CRS and ICANS, discontinuation, and disease course only in aggregate. Trio's extraction captures the qualitative *"why"* at the patient level: CRS management, the cilta-cel neurotoxicity spectrum, reasons for treatment change, relapse patterns, and end-of-life care.

THE QUALITATIVE "WHY" • VERBATIM EVIDENCE, ANONYMIZED

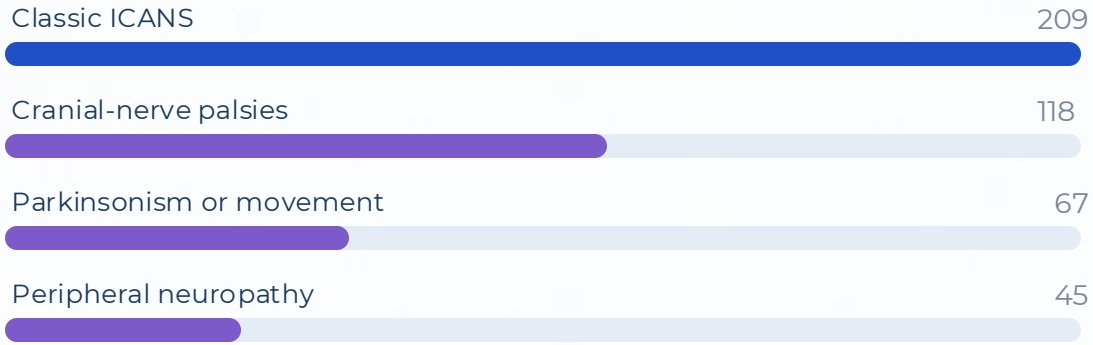
The real-world reflex to CRS and neurotoxicity

Counts show how each event was actually managed or classified in routine care. The quotes are extracted verbatim from the clinical notes.

CRS MANAGEMENT • PATIENT COUNT



NEUROTOXICITY SPECTRUM • PATIENT COUNT



> "Cytokine release syndrome: Max grade 2 (12/18). s/p Toci #1 + 10 mg IV Dex(12/18)"

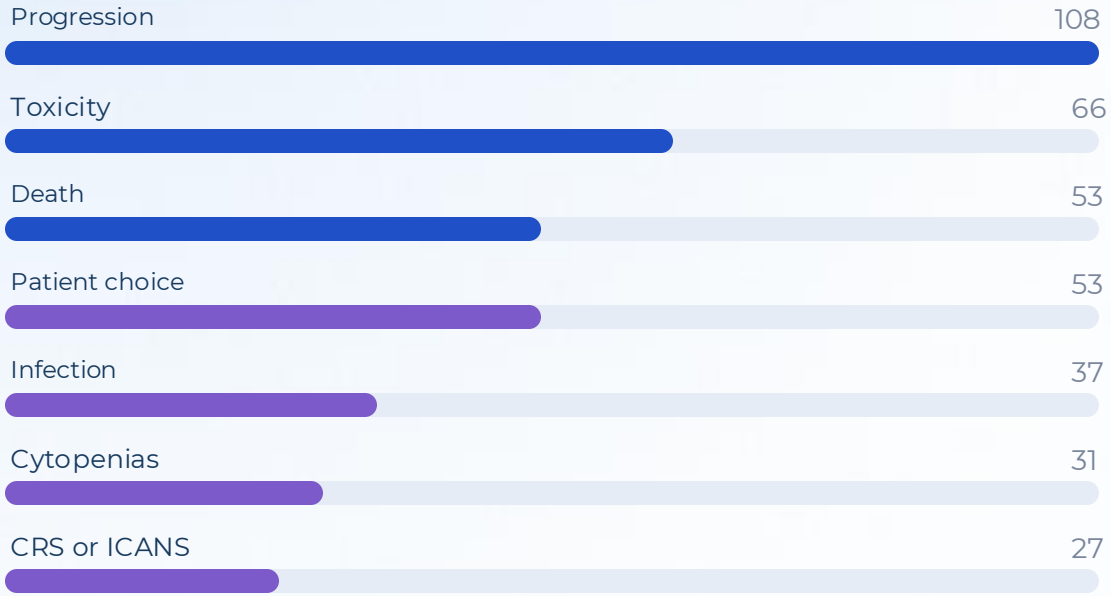
> "Suspected to be a late CAR-T effect with an element ofParkinsonism"

CLINICAL DECISIONS • RELAPSE • END-OF-LIFE

Why therapy stopped, and the course beyond response

Progression led the documented reasons for stopping or changing therapy, followed by toxicity and death. The quotes show the texture trials cannot capture.

REASONS FOR STOPPING OR CHANGING THERAPY • PATIENT COUNT



BRIDGING

"Bridging therapy: S/p Talvey, c/b CRS Grade 1."

RELAPSE

"Received cilta-cel >3 years ago and now havingbiochemical progression."

END-OF-LIFE

"Referral reason: symptom management, goals of care, palliative care."

CONCLUSIONS

A repeatable method for building, validating and using an RRMM cohort

The cohort can be built, and checked

Approximately 17,500 patients confirmed relapsed by reading their notes, and the method recovers 95.4% of known cases when the giveaway drug is hidden from it.

Availability is measurable, and uneven

The facts a trial screens on are the ones least often written down. Reading the notes adds 10 to 14% more patients on top of structured data alone.

The comparison reproduces the trial

Cilta-cel patients went 38.6 months before needing another therapy against 9.4 for matched patients who did not receive it, closely echoing the trial.

The data was always there. **Now we can use it.**