Abstract # 7027

Efficacy of Tocilizumab in Resolving CAR T–Induced CRS: A Pooled Clinical Trial Analysis of Patients with B-cell Lymphoma

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Background and Objective

CAR T therapy
- Offers significant efficacy in Refractory/Relapsed hematologic malignancies.
- But is associated with immune-mediated toxicity, such as Cytokine Release Syndrome (CRS).

Tocilizumab
- An interleukin-6 receptor antagonist.
- The only FDA-approved treatment for CAR T-induced CRS.
- But its efficacy in large patient population remains limited.

Objective: To evaluate tocilizumab efficacy by assessing Complete Response (CR) rates and median time-to-CR in B-cell Lymphoma (BCL) patients experiencing CAR T-induced CRS.

Method

Data Source:
- Patient-level data from **<10 multinational clinical trials** accessed through Medidata Clinical Cloud® were harmonized and aggregated, comprising of 2,304 patients.
- **Inclusion:**
  - Patients with BCL who received CAR T cell treatment.
  - Patients who experienced CAR T cell-induced CRS.
  - Patients who received tocilizumab to treat CRS.
- **Exclusion**:
  - Patients who received siltuximab after CRS and before tocilizumab.

CRS Outcome Definition:

Complete Response (*CR of CRS)	Resolution of CRS within 14 days of the initial tocilizumab dose, characterized by the absence of all Failure to Respond (FR) criterias.
Failure to Respond (FR)	Required more than (>) two doses of tocilizumab
	Required rescue siltuximab
	Escalation of CRS grade after two doses of tocilizumab
	Recurrence of CRS after initially achieving a complete response following two doses of tocilizumab.

Patient Cohort (n=680 met inclusion)

Patients Attrition Criteria	Number of Patients
Total Population, BCL	2304
Patients who received CAR T-cell therapy	1545
Patients who experienced CRS	1098
Patients who were administered with tocilizumab	680

Demographics	
Age in years	61 (53 - 67)
Gender (n, %)	
• Female	251 (36.9%)
• Male	429 (63.1%)
Race (n, %)	
• Asian	37 (5.4%)
• Black or African American	25 (3.7%)
• White	542 (79.7%)
• Unknown/Missing	76 (11.1%)
Ethnicity (n, %)	
• Hispanic or Latino	54 (7.9%)
• Not Hispanic or Latino	586 (86.2%)
• Unknown/Missing	40 (5.9%)
Disease Characteristics	
Indication (n, %)	
• DLBCL	322 (47.4%)
• MCL	90 (13.2%)
• FL	94 (13.8%)
• HGBCL	56 (8.2%)
• TFL	45 (6.6%)
• MZL	53 (7.8%)
• Other	20 (2.9%)
Bulky Disease (n, %)	182 (26.8%)
• Unknown/Missing	39 (5.7%)
Ann Arbor Stage (at the time of Screening)	
• I or II	118 (17.3%)
• III or IV	445 (65.5%)
• Unknown/Missing	117 (17.2%)
ECOG score (prior to CAR-T date)	
• 0	333 (49.0%)
• 1	335 (49.3%)
• >=2	12 (1.8%)

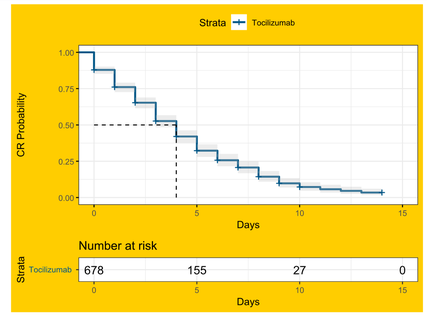
Follow-Up	
Length of Follow-Up in **Months** from Tocilizumab Administration	23.54 (8.42 - 38.15)
Lab Biomarkers	
LDH ukat/L	4.14 (3.27 - 7.53)
Unknown/Missing	229 (33.7%)
CRP mg/L	19.25 (8.47 - 62.30)
Unknown/Missing	336 (49.4%)
Ferritin nmol/L	1.06 (0.58 - 2.49)
Unknown/Missing	203 (29.9%)
Platelet in 10^9/L	125 (80 - 173)
Unknown/Missing	107 (15.7%)
Type of Treatment	
Received Bridging Therapy	236 (34.7%)
Not Received	444 (65.3%)
Type of CAR T Therapy	
• 41BB	184 (27.1%)
• CD28	496 (72.9%)
CRS Events Characteristics	
Onset CRS grade	
1	489 (71.9%)
2	175 (25.7%)
>=3	16 (2.4%)
Maximum CRS grade	
1	236 (34.7%)
2	378 (55.6%)
>=3	56 (9.7%)
Days from CAR T to CRS Onset	2 (1 - 4)
Days from CRS Onset to Tocilizumab Administration	2 (1 - 3)

* Continuous variable is reported in median (IQR)

Tocilizumab achieved a 66% Complete Response (CR) rate in resolving CAR T-induced CRS with a median time-to-CR of 4 days.

Results

Efficacy Outcomes:
- CR Rate = 66% (95% CI: 62.5% – 69.6%)
- Median Time to CR: 4 days (95% CI: 3 – 4)
  - 35% achieved CR in ≤2 days; 80% in ≤7 days



Conclusion

This benchmark analysis validates tocilizumab's role as a first-line therapy for CRS treatment, demonstrating a 66% CR rate and a median 4-day time-to-resolution.

However, the 34% failure rate highlights a critical need for alternative treatment strategies.

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