Poster
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Association of Metabolic Tumor Volume and Clinical Outcomes in Second-Line Relapsed/Refractory Large B-Cell Lymphoma Following Axicabtagene Ciloleucel Versus Standard-of-Care Therapy in ZUMA-7

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is a CD19-directed genetically modified autologous T-cell immunotherapy with a CD28 co-stimulatory domain that provides rapid and strong expansion and reprograms T cells to trigger target-specific cytotoxicity of cancer cells[1,2]
- In the Phase 3 randomized ZUMA-7 (NCT03391466) study, axi-cel showed superiority to standard of care (SOC) across common prognostic subgroups, including high tumor burden (TB), as calculated by the sum of product diameters (SPD), and elevated lactate dehydrogenase (LDH)[3]
- SPD is based on ≤6 target lesions only[3,4] and does not account for non-measured lesions or metabolic activity
- TB can also be measured by metabolic tumor volume (MTV) using fluorodeoxyglucose (FDG) positron emission tomography (PET)-computed tomography (CT) scans
  - Though it is not a standardized clinical assessment, MTV has previously been shown to correlate with clinical outcomes of chimeric antigen receptor (CAR) T-cell therapy in third-line relapsed/refractory (R/R) large B-cell lymphoma (LBCL)[5,6]

OBJECTIVE

- To present clinical outcomes for patients in ZUMA-7 by MTV

METHODS

- In the multicenter Phase 3 ZUMA-7 study, eligible patients were randomized 1:1 to axi-cel or SOC
  - Full ZUMA-7 study details, including primary results, were previously reported[7]
- MTV was obtained from the attenuation-corrected whole-body FDG PET scans performed at screening
- Whole tumor volumes of interest were placed on tumors using a predefined, semiautomated approach
  - Semiautomated approach included semiautomated placement of outlines around regions of abnormal FDG uptake greater than normal liver (visual Deauville score >3) followed by manual adjustments of the lesion contours by the PET radiologist to ensure the inclusion of the entire tumor lesion(s) and/or exclude non-tumorous/normal tissue regions
- Subsequent radiology-defined adjustments of volumes of interest placement were conducted
- MTV was calculated as the number of voxels with standardized uptake value (SUV) measurements between 41%-100% of tumor SUV_{max} and reported as MTV_{total} (mL) per patient
- Associations between MTV and baseline characteristics or clinical outcomes were assessed descriptively (P<.05 was considered significant)

RESULTS

Table 1. Baseline MTV by Treatment Arm and Characteristics

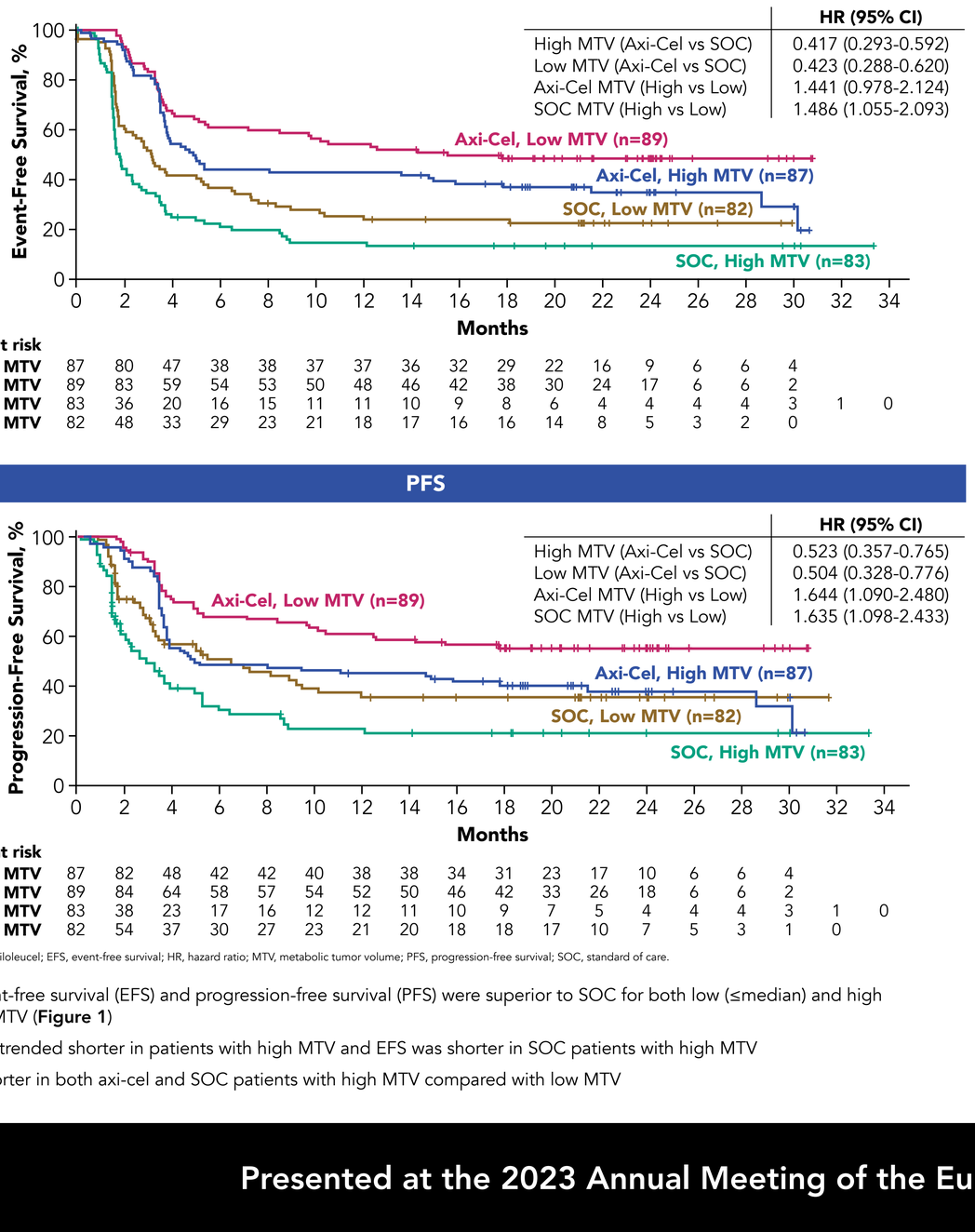
Treatment Arm or Characteristic	n/N[a]	Median MTV (range), mL
Treatment arm		
Axi-Cel	176/180	228.10 (2.3-16,669.3)
SOC	165/179	231.90 (0.04-2811.2)
Age		
<65 years	236/250	255.21 (0.04-16,669.3)
≥65 years	105/109	176.71 (6.8-4101.8)
Molecular subgroup, per central laboratory		
GCB	203/208	228.66 (3.5-16,669.3)
Non-GCB	53/56	242.60 (6.9-5488.5)
Disease type, per central laboratory		
HGBL	54/57	307.71 (8.5-6823.5)
Non-HGBL	252/256	228.03 (0.04-16,669.3)
LDH[b]		
Elevated	185/195	371.17 (2.3-16,669.3)
Normal	156/164	123.92 (0.04-3712.8)
Response to 1L therapy at randomization		
Primary refractory	252/265	236.88 (0.04-16,669.3)
Relapse ≤12 mo after initiation or completion of 1L therapy	88/92	214.85 (3.6-5317.7)
CD19 H-score[c]		
≤median	150/152	241.31 (0.04-16,669.3)
>median	146/151	229.72 (2.3-13,527.0)
CD19 IHC[d]		
Positive	271/278	237.37 (0.04-13,527.0)
Negative	25/25	248.89 (3.6-16,669.3)

[a] n was defined as the number of patients with available MTV data; N was defined as the number of patients in the baseline characteristic cohort.
[b] LDH was quantified at each local clinical laboratory and reported as elevated (≥reference range) or normal (<reference range).
[c] H-score was calculated by the percentage of positive tumor cells (0-100) multiplied by the stain intensity (1-3). Median CD19 H-score was 150.
[d] CD19 IHC was measured using a validated assay at NeoGenomics.
1L, first-line; axi-cel, axicabtagene ciloleucel; GCB, germinal center B-cell–like; HGBL, high-grade B-cell lymphoma; IHC, immunohistochemistry; LDH, lactate dehydrogenase; mo, month; MTV, metabolic tumor volume; SOC, standard of care.

- Overall median MTV was 230.24 mL (range, 0.04-16,669.3)
- Median MTV was similar across treatment arms (**Table 1**)
- MTV was positively correlated with SPD (Spearman correlation=0.5232) and LDH (Spearman correlation=0.4516)

Figure 1. EFS and PFS by MTV and Treatment Arm

EFS



Patients at risk																	
Axi-Cel, High MTV	87	80	47	38	38	37	37	36	32	29	22	16	9	6	6	4	
Axi-Cel, Low MTV	89	83	59	54	53	50	48	46	42	38	30	24	17	6	6	2	
SOC, High MTV	83	36	20	16	15	11	11	10	9	8	6	4	4	4	4	3	1	0
SOC, Low MTV	82	48	33	29	23	21	18	17	16	16	14	8	5	3	2	0		

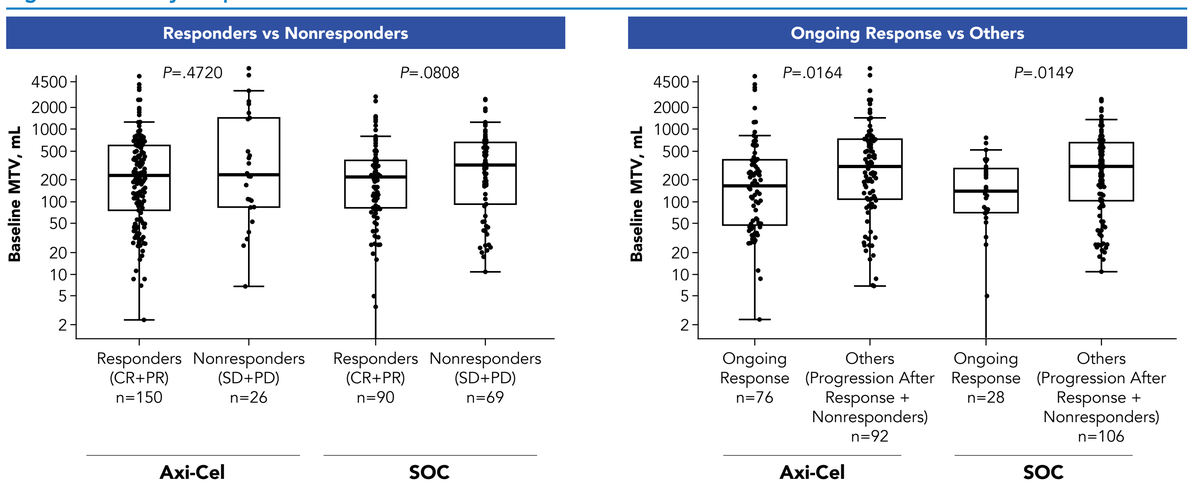
PFS

Patients at risk																	
Axi-Cel, High MTV	87	82	48	42	42	40	38	38	34	31	23	17	10	6	6	4	
Axi-Cel, Low MTV	89	84	64	58	57	54	52	50	46	42	33	26	18	6	6	2	
SOC, High MTV	83	38	23	17	16	12	12	11	10	9	7	5	4	4	4	3	1	0
SOC, Low MTV	82	54	37	30	27	23	21	20	18	18	17	10	7	5	3	1	0	

Axi-cel, axicabtagene ciloleucel; EFS, event-free survival; HR, hazard ratio; MTV, metabolic tumor volume; PFS, progression-free survival; SOC, standard of care.

- Axi-cel event-free survival (EFS) and progression-free survival (PFS) were superior to SOC for both low (≤median) and high (>median) MTV (**Figure 1**)
- Axi-cel EFS trended shorter in patients with high MTV and EFS was shorter in SOC patients with high MTV
- PFS was shorter in both axi-cel and SOC patients with high MTV compared with low MTV

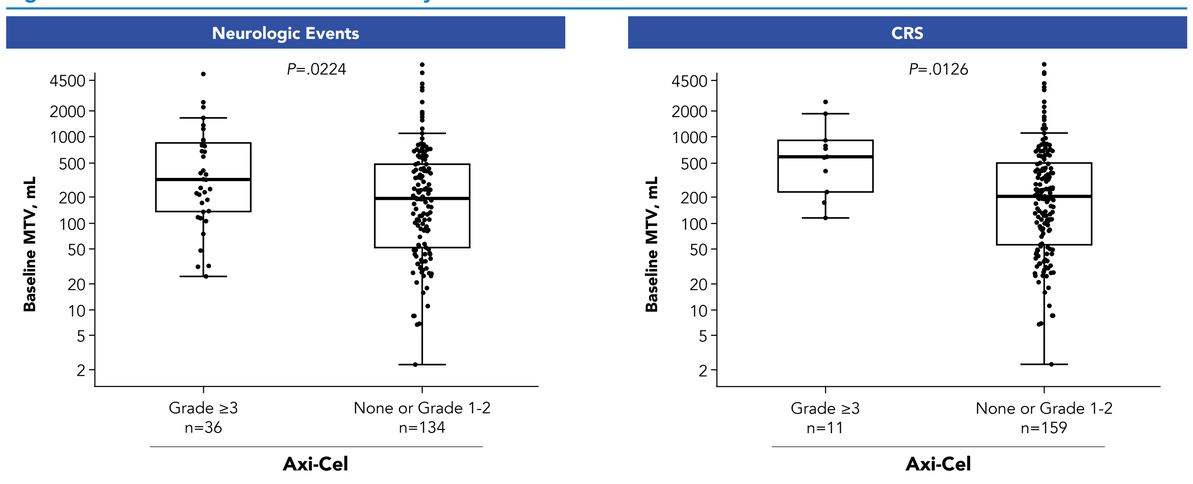
Figure 2. MTV by Response and Treatment Arm



Axi-cel, axicabtagene ciloleucel; CR, complete response; MTV, metabolic tumor volume; PD, progressive disease; PR, partial response; SD, stable disease; SOC, standard of care.

- In the axi-cel arm, median MTV was similar between responders (complete response [CR] + partial response [PR]) and nonresponders (stable disease [SD] + progressive disease [PD]; **Figure 2**)
- MTV was lower in patients treated with axi-cel who were in ongoing response compared with others (progression after response + nonresponders)
- MTV trended lower in patients with CR compared with others (PR, SD, and PD; data not shown)
  - Notably, by logistic regression, a negative association was observed between CR and MTV in both axi-cel and SOC arms

Figure 3. Association of MTV With Toxicity in the Axi-Cel Arm



Axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; MTV, metabolic tumor volume.

- In the axi-cel arm, median MTV was higher in patients who experienced Grade ≥3 neurologic events or cytokine release syndrome (CRS) compared with patients who experienced Grade 1-2 or no neurologic events or CRS, respectively (**Figure 3**)
- No associations of MTV and safety were observed for the SOC arm

CONCLUSIONS

- To our knowledge, this analysis is the first to examine the relation between MTV and clinical outcome in a large, randomized, prospective R/R LBCL study of CAR T-cell therapy
- Similar to previous analysis with SPD- and LDH-based subgroups,[3] axi-cel was superior to SOC for both high and low MTV groups
- While TB per SPD did not seem to impact axi-cel outcomes in ZUMA-7,[3] low MTV was associated with improved outcomes with axi-cel versus high MTV, and rates of Grade ≥3 neurologic events and CRS were associated with higher MTV
- These findings suggest that MTV may be a better prognostic marker than SPD

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- †Current affiliation: US Department of Veterans Affairs; Dr. Cheng was an employee of Kite when the studies reported here were conducted
- These data were previously presented at the 2022 Annual Meeting of the American Society of Hematology[8]

DISCLOSURES

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Full author disclosures are available through the Quick Response (QR) code

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