606 **IMPOWER110: TERTIARY LYMPHOID STRUCTURES (TLS) AND CLINICAL OUTCOMES IN ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC) TREATED WITH FIRST-LINE ATEZOLIZUMAB OR CHEMOTHERAPY**

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Background The presence of TLS in tumor tissues is associated with good prognosis and increased immunotherapy sensitivity across several cancers. In an analysis of samples from the Phase II POPLAR trial of atezolizumab vs chemotherapy in previously treated NSCLC, the presence of TLS was strongly associated with atezolizumab OS benefit. IMpower110 (NCT02409342) was a Phase III study of first-line atezolizumab vs chemotherapy in PD-L1-selected NSCLC. We describe results of pathologist-identified TLS status and its association with clinical outcomes in IMpower110.

Methods Chemotherapy-naive patients with metastatic SP142 PD-L1+ (≥1% positive on tumor or tumor-infiltrating immune cells [TC1/2/3 or IC1/2/3]) NSCLC were randomized (1:1) to atezolizumab or chemotherapy IV q3w. Digital images of baseline IMpower110 hematoxylin- and eosin-stained (H&E) samples were reviewed by ≥2 pathologists, per a standard protocol, for the presence of dense lymphoid aggregates (LA) with ≥1 distinct germinal center (TLS), without any germinal centers (LA), or the absence of both (neither). Samples with poor image or tissue quality, cytology collections, and lymph-node samples were excluded.

Results Of 572 intention-to-treat patients, 422 comprised the TLS biomarker-evaluable population (TLS-BEP). Similar TLS distributions were seen across treatment arms, SP142 PD-L1 status, and patient-level histology. Within the atezolizumab arm, OS benefit was greatest in the TLS, followed by the LA, and then the neither groups. PFS benefit within the atezolizumab arm was greater in the TLS than LA or neither groups. Within the chemotherapy arm, OS but no PFS benefit was observed in the TLS vs the LA or neither groups. In comparing atezolizumab vs chemotherapy, PFS benefit with atezolizumab was observed irrespective of TLS status; however, the OS benefit of atezolizumab was seen only in the TLS and LA groups (TLS-BEP; table 1). Within the SP142 PD-L1-high (TC3 or IC3) population, OS and PFS benefit with atezolizumab vs chemotherapy trended across TLS subgroups. In the SP142 PD-L1-intermediate or low (TC1/2 or IC1/2) population, survival benefit with atezolizumab vs chemotherapy was observed in the TLS (PFS and OS) and LA (OS only) groups.

Conclusions This exploratory analysis represents the first large-scale TLS/LA study in advanced NSCLC in the context of a randomized clinical trial of immune checkpoint blockade vs chemotherapy in the first-line setting. H&E assessment was sufficient to identify mature and immature lymphoid structures. The presence of TLS in tumor tissues may identify a subset of patients that benefits from atezolizumab monotherapy in the PD-L1-intermediate or low population.

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Trial Registration NCT02409342

Ethics Approval IMpower110 was conducted in full accordance with Good Clinical Practice guidelines and the Declaration of Helsinki or the laws and regulations of the country in which the research was conducted, whichever afforded the most protection. The protocol was approved by independent ethics committees for each site. Written informed consent was obtained from all the patients.

Abstract 606 Table 1

TLS status	Atezo, n	Chemo, n	OS HR (95% CI) Median OS, mo (atezo vs chemo)	PFS HR (95% CI) Median PFS, mo (atezo vs chemo)
TLS-BEP				
TLS	33	29	0.50 (0.21, 1.20) NR vs 17.5	0.49 (0.25, 0.96) 15.3 vs 5.6
LA	80	71	0.60 (0.38, 0.94) 17.6 vs 12.5	0.69 (0.47, 1.01) 5.7 vs 5.7
Neither	105	104	0.87 (0.60, 1.26) 12.4 vs 13.1	0.64 (0.45, 0.91) 5.7 vs 4.9
SP142 PD-L1–high (TC3 or IC3) TLS-BEP				
TLS	15	10	0.48 (0.16, 1.51) NR vs 17.5	0.54 (0.21, 1.42) 20.3 vs 3.4
LA	28	21	0.51 (0.25, 1.03) 17.4 vs 9.1	0.49 (0.25, 0.94) 10.7 vs 5.7
Neither	41	38	0.78 (0.46, 1.34) 19.5 vs 13.1	0.48 (0.29, 0.79) 7.3 vs 4.2
SP142 PD-L1–intermediate or low (TC1/2 or IC1/2) TLS-BEP				
TLS	18	19	0.57 (0.21, 1.57) NR vs 17.0	0.44 (0.2, 0.97) 10.0 vs 6.0
LA	52	50	0.79 (0.49, 1.29) 18.9 vs 14.1	1.00 (0.67, 1.49) 4.9 vs 5.6
Neither	64	66	1.04 (0.69, 1.55) 11.2 vs 13.6	0.80 (0.55, 1.16) 5.6 vs 5.5

Atezo, atezolizumab; chemo, chemotherapy; NR, not reached; OS, overall survival; PFS, progression-free survival.

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