Final Results from TAIL: Updated Long-Term Safety and Efficacy of Atezolizumab in a Diverse Population of Patients With Previously Treated Advanced NSCLC

Abstract #316
Poster #9P

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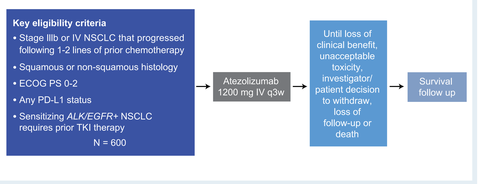
BACKGROUND

- First-line (1L) treatment options for patients with non-small cell lung cancer (NSCLC) include immune checkpoint inhibitor (CPI) monotherapy, such as anti–programmed death-ligand 1 (PD-L1) antibody therapies for those with high tumour expression of PD-L1, as well as chemo-immunotherapy combinations[1]
  - For patients with previously treated NSCLC, anti–PD-L1/anti–programmed cell death protein 1 (PD-1) antibody therapies are the standard of care in the second-line and beyond setting[1,2]
- Atezolizumab (anti–PD-L1) monotherapy is approved to treat patients with locally advanced or metastatic NSCLC that progressed during or following platinum-containing chemotherapy[3,4]
- In the OAK study (NCT02008227) atezolizumab monotherapy significantly improved overall survival (OS) vs docetaxel. In the intent-to-treat population median OS improved to 13.8 months in the atezolizumab arm compared with 9.6 months in the docetaxel arm (hazard ratio [HR], 0.73; 95% CI: 0.62, 0.87; *P*=0.0003)[5]
- Clinical trials of anti–PD-L1/PD-1 therapies typically exclude patients outside OAK study eligibility criteria, including patients with Eastern Cooperative Oncology Group performance status (ECOG PS) 2; previous anti–PD-1, anti–PD-L1 or anti–CTLA-4 therapy; untreated central nervous system (CNS) metastases; creatinine clearance <30 mL/min; liver abnormality; active or chronic hepatitis B or hepatitis C (HBV/HCV) infection; autoimmune disease or systemic steroid treatment[6-8]
  - Clinicians need more data to guide cancer immunotherapy treatment decisions for these patients, who are often encountered in real-world clinical practice
- TAIL (NCT03285763) is a global single-arm study of atezolizumab monotherapy in patients from a diverse population with previously treated NSCLC that more closely reflects the real world, which expanded the eligibility criteria to include patients with:
  - Prior treatment with CPIs, such as anti–PD-1, anti–PD-L1 or anti–CTLA-4 therapy
  - Untreated asymptomatic CNS metastases
  - Autoimmune disease
  - ECOG PS 2
  - Renal impairment
  - Active or chronic HBV/HCV infections
- At the primary analysis, the co-primary endpoints, treatment-related (TR) serious adverse events (SAEs) and TR immune-related adverse events (irAEs), occurred in 7.8% and 8.3% of patients, respectively[9]
- Here the final safety and efficacy data from TAIL are presented

METHODS

- TAIL (NCT03285763) is a prospective, phase III/IV, open-label, single-arm, multicentre study conducted in patients with locally advanced or metastatic NSCLC with disease progression following standard chemotherapy (Figure 1)
- Patients with any PD-L1 status were eligible, as were patients with treated or untreated asymptomatic CNS metastases, autoimmune disease, ECOG PS 2, positive for human immunodeficiency virus or active/chronic HBV/HCV, severe renal impairment and prior anti–PD-1 therapy
- Patients received 1200 mg IV atezolizumab on Day 1 of each 21-day cycle until radiographic disease progression (PD) per RECIST 1.1
- The primary endpoint was safety as measured by the incidence of TR SAEs and TR irAEs
  - irAEs were defined as adverse events of special interest (AESI) requiring corticosteroid treatment within 30 days of onset
- Key secondary and exploratory endpoints included OS, Progression free survival (PFS), Overall response rate (ORR) and Duration of response (DOR)
- Safety and efficacy in key patient subgroups were also assessed
- Clinical cutoff for the final analysis was approximately 30 months after the last patient was enrolled

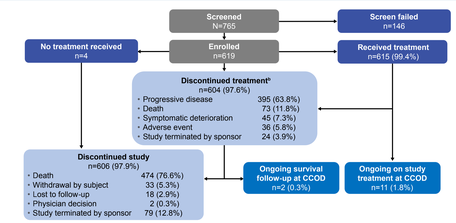
Figure 1. TAIL study design



RESULTS

- 615 patients received atezolizumab treatment and were included in the primary analysis set; 4 patients died before initiating treatment (Figure 2)
- At data cutoff (26 June 2021), the median survival follow-up was 36.1 months (range, 0.0-42.3 months)
- The study population included patients with ECOG PS 2 (9.9%), renal impairment (12.8%), history of autoimmune disease (4.9%), active or chronic HBV/HCV (2.3%), prior anti–PD-1 therapy (6.5%) or CNS metastases (14.6%) at baseline (Table 1)

Figure 2. Patient disposition[a]



CCOD, clinical cutoff date.
[a]CCOD was 26th June 2021. [b]All reasons for patient discontinuation of treatment are not listed.

Table 1. Demographic and baseline characteristics

n (%)	Atezolizumab (N=615)
Age	
Median (range), years	64.0 (24-88)
≥75 years	76 (12.4)
Sex	
Male	370 (60.2)
Female	245 (39.8)
Smoking status	
Never	127 (20.7)
Current/previous	488 (79.3)
Race	
White	483 (78.5)
Asian	76 (12.4)
American Indian or Alaska Native	44 (7.2)
Black or African American	4 (0.7)
Other[a]	6 (1.0)
Unknown	2 (0.3)
ECOG PS[b]	
0	193 (31.4)
1	361 (58.7)
2	61 (9.9)
eGFR at baseline,[c] mL/min/1.73 m²	
15 to <30	2 (0.3)
30 to <60	77 (12.5)
60 to <90	251 (40.8)
≥90	283 (46.0)
Missing	2 (0.3)
Autoimmune disease	30 (4.9)
Active/chronic HBV/HCV[d]	14 (2.3)
Prior CPI	
Any anti–CTLA-4	1 (0.2)
Any anti–PD-1	40 (6.5)
CNS metastases	90 (14.6)

eGFR, estimated glomerular filtration rate.
[a]Other includes multiple race as well as Native Hawaiian or other Pacific Islander. [b]Baseline evaluation is defined as the latest evaluation performed prior to or on the first dosing date. [c]Defined as an eGFR of <60 mL/min/1.73 m² using the Chronic Kidney Disease Epidemiology Collaboration equation. [d]Active and chronic HBV/HCV is defined as active and chronic hepatitis B or anti-hepatitis C antibody positive and hepatitis C core antigen not negative and ongoing hepatitis C reported as medical history.

Safety

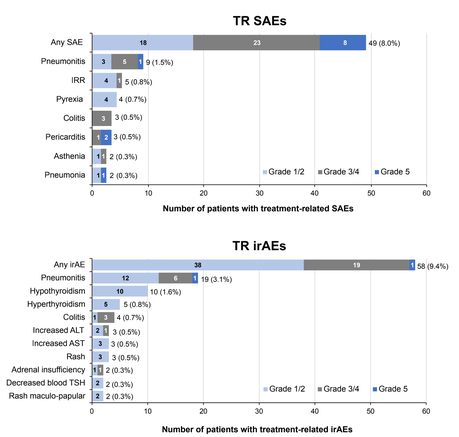
- Treatment duration is shown in Table 2

Table 2. Treatment duration

	Atezolizumab (N=615)
Treatment duration (range), months	3.15 (0.0-42.3)
Treatment duration, n (%)	
≤3 months	303 (49.3)
>3 to ≤6 months	93 (15.1)
>6 to ≤12 months	97 (15.8)
>12 months	122 (19.8)
No. of cycles initiated	
Median (minimum, maximum)	5.0 (1, 60)

- TR SAEs and TR irAEs occurred in 8.0% (95% CI: 6, 10) and 9.4% (95% CI: 7, 12) of patients, respectively (Figure 3)
- The most common Grade ≥3 TR SAEs were pneumonitis, pericarditis and colitis (Figure 3)
  - Pneumonitis was the only Grade 3 or higher TR SAE (1.0%) and TR irAE (1.1%) that occurred in ≥1% of patients
  - The majority of TR irAEs were Grade 1 or 2 in severity

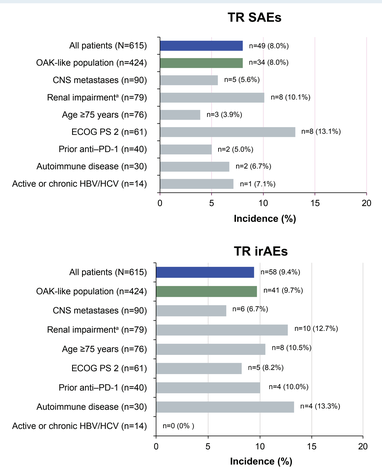
Figure 3. Primary endpoint: most common TR SAEs and irAEs (by PT, ≥2 patients)



ALT, alanine aminotransferase; AST, aspartate aminotransferase; IRR, infusion-related reaction; TSH, thyroid-stimulating hormone; PT, preferred term.
Investigator text for AEs encoded using MedDRA version 24.0. All counts represent number of patients. Multiple occurrences of the same AE in 1 individual are counted once at the highest grade for that patient. AEs started on or after the first dose of the study drug are included. irAEs are defined as AESIs associated with systemic corticosteroid use within 30 days of the onset date.

- Safety data for the subgroups were similar to those for the overall population, despite a moderately higher incidence of TR SAEs in the ECOG PS 2 subgroup (13.1%; n=8/61) vs the overall population (Figure 4)
- For TR irAEs, safety data for the subgroups were similar to those for the overall population, with the exception of a moderately higher incidence in the renal impairment subgroup (12.7%; n=10/79) vs the overall population (Figure 4)
- Due to the relatively small group size in the ECOG PS 2 (n=61) and renal impairment (n=79) subgroups, no clinically meaningful conclusions could be drawn

Figure 4. TR SAEs and irAEs by subgroup

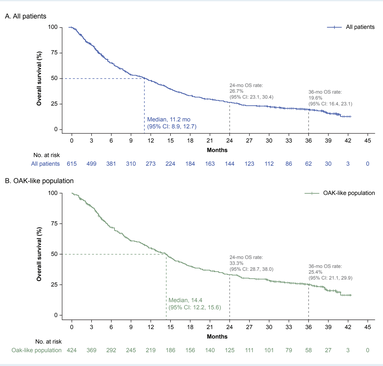


[a]Renal impairment is defined as eGFR <60 mL/1.73 m².

Efficacy

- The median duration of survival follow-up was 36.1 months (95% CI: 34.9, 38.0)
- In the final analysis, the median OS was 11.2 months (95% CI: 8.9, 12.7) (Figure 5A)
- The median OS of the OAK-like population was 14.4 months (95% CI: 12.2, 15.6) (Figure 5B)

Figure 5. Median OS



- Overall survival results for the subgroups are presented in Table 3

Table 3. Efficacy by OS in subgroups

	Median (95% CI), months	12-month OS rate (95% CI), %	24-month OS rate (95% CI), %	36-month OS rate (95% CI), %
All patients (N=615)	11.2 (8.9, 12.7)	47.9 (43.8, 51.9)	26.7 (23.1, 30.4)	19.6 (16.3, 23.1)
Age				
≥75 years (n=76)	11.8 (7.9,14.7)	47.1 (35.2, 58.1)	22.2 (13.3, 32.5)	17.5 (9.5, 27.4)
Sex				
Male (n=370)	11.5 (8.7, 13.3)	48.3 (43.0, 53.4)	28.3 (23.7, 33.1)	19.7 (15.6, 24.3)
Female (n=245)	10.7 (8.1, 13.0)	47.2 (40.6, 53.4)	24.1 (18.7, 30.0)	19.5 (14.4, 25.1)
Histological subtype[a]				
Non-squamous (n=461)	10.4 (8.4, 12.6)	46.5 (41.7, 51.1)	27.2 (23.0, 31.5)	20.2 (16.4, 24.3)
Squamous (n=153)	12.5 (8.9, 14.1)	51.5 (43.2, 59.2)	24.8 (18.1, 32.0)	17.1 (11.4, 23.9)
ECOG PS at baseline				
0/1 (n=554)	12.4 (10.7, 14.1)	50.7 (46.4, 54.9)	29.0 (25.1, 33.0)	21.4 (17.8, 25.1)
2 (n=61)	3.5 (1.9, 5.0)	21.5 (12.0, 32.8)	5.4 (1.4, 13.4)	3.6 (0.7, 10.9)
CNS metastases (n=90)	5.1 (3.9, 8.1)	24.3 (15.6, 34.1)	10.2 (4.8, 18.1)	7.5 (3.0, 14.7)
Liver metastases (n=136)	4.6 (3.7, 5.7)	25.3 (18.1, 33.1)	13.1 (7.9, 19.6)	6.3 (2.9, 11.6)
Autoimmune disease (n=30)	10.1 (6.5, 14.1)	44.9 (26.6, 61.6)	17.3 (6.3, 32.8)	6.9 (1.2, 19.8)
Prior anti–PD-1 therapy (n=40)	5.8 (3.3, 11.5)	31.9 (18.0, 46.8)	8.0 (2.1, 19.3)	NE (NE, NE)
Renal impairment (n=79)[b]	11.9 (8.5, 15.3)	48.2 (36.8, 58.8)	25.6 (16.4, 35.7)	15.8 (8.6, 25.1)
EGFR positive (n=40)[c]	8.7 (5.2, 15.7)	35.8 (20.5, 51.4)	19.9 (8.3, 35.0)	15.9 (5.6, 30.9)
ALK positive (n=5)	20.0 (2.8, NE)	75.0 (12.8, 96.1)	25.0 (0.9, 66.5)	NE (NE, NE)
BEP				
Yes (n=381)	11.1 (8.3,12.7)	46.8 (41.6, 51.8)	25.1 (20.7, 29.8)	17.8 (13.9, 22.1)
PD-L1 expression on TC (BEP)				
Positive (≥1%) (n=213)	12.6 (8.7,14.8)	50.3 (43.2, 57.0)	29.2 (22.9, 35.7)	20.5 (15.0, 26.7)
Negative (<1%) (n=168)	8.7 (6.3,11.9)	42.4 (34.8, 49.8)	20.3 (14.5, 26.8)	14.4 (9.3, 20.6)
PD-L1 expression on TC (BEP)—OAK-like				
Positive (≥1%) (n=147)	15.5 (14.2, 21.7)	59.8 (51.2, 67.5)	38.4 (30.1, 46.5)	28.4 (20.9, 36.4)
Negative (<1%) (n=111)	11.7 (7.9, 13.7)	48.7 (39.0, 57.7)	23.9 (16.3, 32.4)	19.1 (12.0, 27.5)

BEP, biomarker-evaluable population; NE, not evaluable; TC, tumour cell.
[a]One patient was missing data. [b]eGFR <60 mL/min/1.73 m². [c]EGFR positive status includes any EGFR mutation (L858R or Ex.19 deletion, other).

CONCLUSIONS

- The data cutoff date for this analysis per protocol was 30 months after the last patient was enrolled
- Based on this updated data, despite the limited number of patients in each subgroup, TAIL demonstrated that atezolizumab monotherapy has a favourable risk-benefit ratio in patients with NSCLC who have been previously treated (eg, patients who received prior anti–PD-1 treatment or have pre-existing autoimmune disease), and the results are generally consistent with published data related to CPI use in special interest populations (eg, patients with ECOG PS 2[10])
- Our study provides novel data on the use of atezolizumab in a more diverse population, which can inform treatment decisions in patients generally excluded from pivotal NSCLC trials
- These updated data confirm a positive risk-benefit ratio for atezolizumab in the prior-treated NSCLC setting and may prove useful for informing treatment decisions in patients generally excluded from pivotal NSCLC trials

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DISCLOSURES

- AA: Eli-Lilly, BMS, MSD, Roche, AZ, Takeda, Bayer (advisory board)
- The corresponding author, Dr Ardizzoni, may be contacted at andrea.ardizzoni@aosp.bo.it.

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer. V1.2022.
2. Planchard D, et al. *Ann Oncol* 2018;29(suppl 4):iv192-237.
3. Tecentriq (atezolizumab). Package insert. Genentech, Inc; 2021.
4. Tecentriq (atezolizumab). Summary of product characteristics. Roche Pharma AG; 2021.
5. Rittmeyer A, et al. *Lancet* 2017;389:255-65.
6. Brahmer J, et al. *N Engl J Med* 2015;373:123-35.
7. Borghaei H, et al. *N Engl J Med* 2015;373:1627-39.
8. Leighl NB, et al. *Lancet Respir Med* 2019;7:347-57.
9. Ardizzoni A, et al. *J Immunother Cancer* 2021;9:e001865.
10. Spigel DR, et al. *J Thorac Oncol* 2019;14:1628-39.

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