Poster 326E

Durvalumab ± tremelimumab + chemotherapy in 1L metastatic NSCLC: overall survival update from POSEIDON after median follow-up of approximately 4 years


Introduction

In the Phase 3 POSEIDON study, 1L T+DCT demonstrated improved progression-free survival (PFS) in OS vs CT alone in patients with mNSCLC:

- OS (HR 0.75; 95% CI 0.63–0.88; p<0.001; median follow-up 42 months in combined patients)
- DCT showed a statistically significant improvement in PFS and a positive trend for OS improvement vs CT that was not significant in relation to HR (0.80; 95% CI 0.62–1.04).

Methods

Patients were randomised (1:1:1) to 1L treatment with:

- T + D 75 mg Q + 1350 mg CT q3w for 4 cycles, followed by D plc maintenance until PD, with one additional dose of T post-week 16; 9th dose)
- D+CT q4w for 4 cycles, then D plc maintenance until PD, or CT q3w for up to 8 cycles (Figure 1).

Results and interpretation

- Across patient subgroups, OS benefit was generally consistent with the ITT population.
- In the Phase 3 POSEIDON study, 1L T+D+CT demonstrated

Objective

- To report an updated analysis of OS after a median follow-up of approximately 4 years, including updated analyses of OS by histology (mNGS or IHC) and STKIT+ ARKO molar status (m vs ctDNA).

Conclusions

- Across patient subgroups, OS benefit was generally consistent with the ITT population.
- OS benefit with T+D+CT vs CT appeared more pronounced in patients with NSQ than SQ histology.
- No new safety signals were observed in the long-term follow-up of various RAs.
- Data from the same treatment options in patients who had not previously received treatment for metastatic NSCLC (tremelimumab or chemotherapy; durvalumab plus chemotherapy; durvalumab alone; or chemotherapy alone).
- Previously presented results from POSEIDON: based on monitoring participants in the clinical study for nearly 3 years, showed that participants who received tremelimumab plus durvalumab and chemotherapy had a better chance of living longer than those who received chemotherapy alone. In addition, participants treated with durvalumab plus chemotherapy may have had an improved chance of living longer than participants treated with chemotherapy alone, but the results were not statistically significant.

Updated survival results from the POSEIDON study were assessed after participants had been monitored for nearly 4 years, to help understand how the different treatment options worked over the long term, and to check whether there were any serious side effects from receiving the drugs over an extended period of time.

The updated results showed that participants who received tremelimumab plus durvalumab and chemotherapy continued to have an improved chance of living longer than those who received chemotherapy—nearly as many participants survived for at least 3 years when treated with tremelimumab plus durvalumab and chemotherapy compared with chemotherapy alone.

The results for participants treated with durvalumab plus chemotherapy were consistent with the previously presented data. There were no new serious safety issues during the entire period of monitoring the study.

These findings suggest that tremelimumab plus durvalumab and chemotherapy is a potential new treatment option for previously untreated patients with metastatic NSCLC.

Results and interpretation

- In this updated analysis, after a median follow-up of 4.5 months, demonstrate the durable long-term OS benefit of adding a limited course of T (Uniplet PD) and 4 cycles of CT OS HR vs CT 0.75 (0.63–0.88). There were no new safety signals observed in the long-term follow-up of various RAs.
- Across patient subgroups, OS benefit was generally consistent with the ITT population.
- OS benefit with T+D+CT vs CT appeared more pronounced in patients with NSQ than SQ histology.
- No new safety signals were observed in the long-term follow-up of various RAs.
- Data from the same treatment options in patients who had not previously received treatment for metastatic NSCLC (tremelimumab or chemotherapy; durvalumab plus chemotherapy; durvalumab alone; or chemotherapy alone).
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Plain language summary

POSEIDON was a phase 3 clinical study in patients with a type of lung cancer called non-small-cell lung cancer (mNSCLC), which has spread to other parts of the body (metastatic mNSCLC). The study compared three different treatment options in patients who had not previously received treatment for metastatic NSCLC (tremelimumab plus chemotherapy; durvalumab plus chemotherapy; or chemotherapy alone).

Previously presented results from POSEIDON: based on monitoring participants in the clinical study for nearly 3 years, showed that participants who received tremelimumab plus durvalumab and chemotherapy had a better chance of living longer than those who received chemotherapy alone. In addition, participants treated with durvalumab plus chemotherapy may have had an improved chance of living longer than participants treated with chemotherapy alone, but the results were not statistically significant.

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These findings suggest that tremelimumab plus durvalumab and chemotherapy is a potential new treatment option for previously untreated patients with metastatic NSCLC.

Methods

• Patient tumours were molecularly characterised via sequencing of tissue and/or ctDNA.

• Consistent with an earlier analysis, in the subgroup of ET patients who received NSQ tumours, a trend for OS benefit was observed for T+D+CT vs CT alone at the updated DCO HR 0.42; 95% CI 0.25–0.70 (Figure 1).• Due to the lower prevalence of KEAP1 mutations, OS in the KEAP1 subgroup was assessed imprecisely (n=1); an interim OS benefit continued to be observed for T+D+CT vs CT (HR 0.74; 95% CI 0.59–1.00), although the small sample size should be noted (Figure 5).• In patients with ALK NSQ tumours, a trend for OS benefit was observed for T+D+CT vs CT alone at the updated DCO HR 0.8; 95% CI 0.6–1.1 (Figure 1).• Among 152 patients with XRA5 NSQ tumours, a trend for extended OS benefit was observed for T+D+CT vs CT alone (HR 0.85; 95% CI 0.63–1.11) (Figure 5).• No new safety signals were identified based on the collection of toxicity data during long-term follow-up (Supplementary Table 3B, available on the QR code).