Impact of mutation status in the TOPAZ-1 study of durvalumab plus gemcitabine and cisplatin in advanced biliary tract cancer

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Summary

What is this poster about?

This poster summarises the results from an analysis of the Phase 3 TOPAZ-1 clinical study looking at treatment with durvalumab (immunotherapy) combined with gemcitabine and cisplatin (chemotherapy) for people with advanced biliary tract cancer (BTC). In BTC, changes in the DNA sequence of a person's tumour cells, known as genetic alterations, are common. Some types of alterations in a person's tumour may make it susceptible to treatment with a targeted cancer therapy. These are known as clinically actionable alterations. Several clinically actionable alterations have been identified in tumours from people with BTC. The purpose of this exploratory analysis was to identify the most common tumour alterations in participants with advanced BTC from the TOPAZ-1 study and to find out if certain alterations affect how well durvalumab plus chemotherapy worked

What were the results of the study?

The most common alterations found in this analysis were similar to alterations that have been found in other studies of people with BTC. The percentage of participants with the most common alterations in this analysis varied by the type of BTC and by where participants lived in the world. Participants whose tumours had the most common alterations in this analysis generally benefitted from treatment with durvalumab plus chemotherapy when compared with placebo plus chemotherapy

What do the results of the study mean?

The treatment combination of durvalumab plus chemotherapy may help to prolong the lives of people with advanced BTC, regardless of the specific alterations in their tumours. Further studies are required to confirm these findings

Where can I access more information?

The primary results of the TOPAZ-1 study can be found here: https://evidence.nejm.org/doi/full/10.1056/EVIDoa2200015

The full oral presentation of the TOPAZ-1 tumour mutations analysis can be found here: https://oncologypro.esmo.org/meeting-resources/esmo-asia-congress/impact-of-mutation-status-on-efficacy-outcomes-in-topaz-1-a-phase-iii-study-of-durvalumab-d-or-placebo-pbo-plus-gemcitabine-and-cisplatin-gc

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Poster

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What is the TOPAZ-1 study?

- BTC includes cancer of the bile ducts or gallbladder. People with BTC that cannot be treated by surgery have advanced BTC
- The anti-cancer treatment durvalumab is a type of immunotherapy. Immunotherapy is a treatment that helps the body's own immune system to recognise and kill cancer cells
- The Phase 3 clinical study TOPAZ-1 showed that participants with advanced BTC who were treated with durvalumab plus chemotherapy lived significantly longer than those who were treated with placebo plus chemotherapy
- Based on these results, durvalumab plus chemotherapy is approved in the United States, Europe, Japan, and several other countries for people with previously untreated advanced BTC
- The purpose of this exploratory analysis was to identify the most common tumour alterations in participants with advanced BTC from the TOPAZ-1 study and to find out if certain alterations affect how well durvalumab plus chemotherapy worked

How was this analysis carried out?

Figure 1. Overview of analysis

Who was included in the TOPAZ-1 study?

685
adults who had not received previous treatment for advanced BTC or those whose disease had come back after curative surgery

Who was included in this analysis?

441
participants from the TOPAZ-1 study had a tumour sample that could be tested for genetic alterations

What treatment did participants get in this analysis?

214
participants were included in the durvalumab plus chemotherapy group

227
participants were included in the placebo plus chemotherapy group

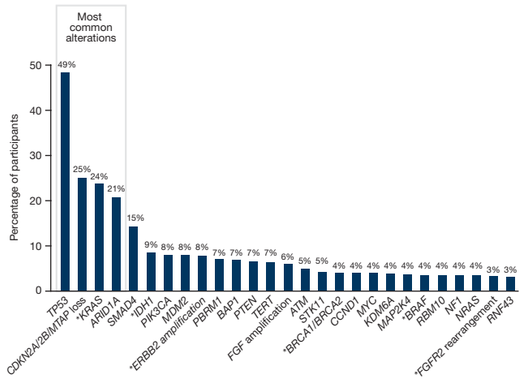
What was measured in this analysis?

- The percentage of participants with alterations
- The reduction in the risk of death for participants taking treatment
- The reduction in the risk that a participant's cancer grew, spread, or got worse after treatment
- The percentage of participants whose cancer shrank or disappeared after treatment

What were the results of this analysis?

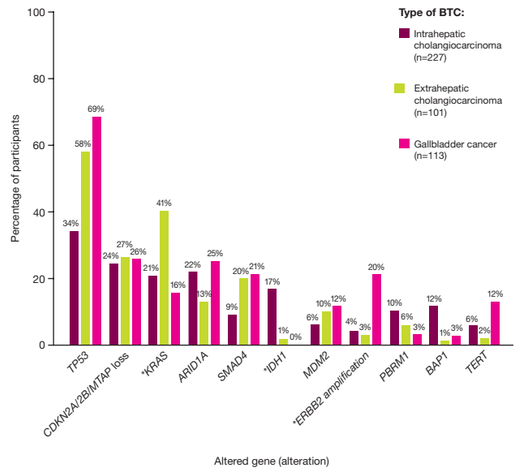
- The most common alterations (>20% participants) were *TP53* (49%), *CDKN2A/2B/MTAP* loss (25%), *KRAS* (24%), and *ARID1A* (21%) (Figure 2)
- The percentage of participants with alterations varied by the type of BTC (Figure 3)
- The majority of the most common alterations identified in the study were found across all types of BTC (Figure 3)

Figure 2. Percentage of participants with alterations



Alterations found in ≥3% of participants are shown. Percentages are calculated out of 441 participants included in the analysis.
*Clinically actionable alterations.

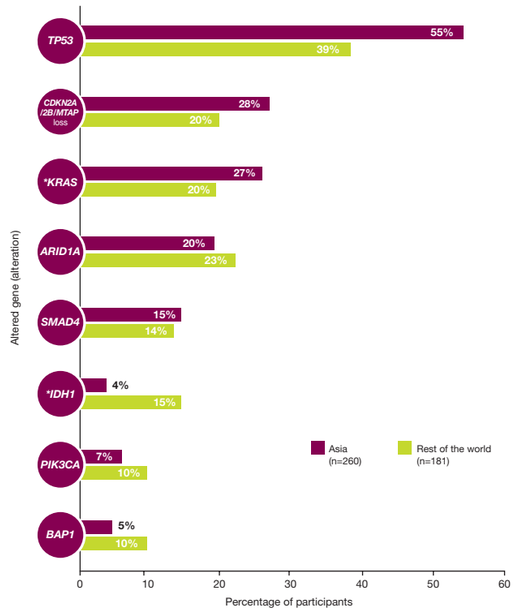
Figure 3. Percentage of participants with alterations by type of BTC



*Clinically actionable alterations.

- Around half of the participants in TOPAZ-1 were treated in Asia. The most common alterations identified in the study were found in participants treated in both Asia and the rest of the world (Figure 4)

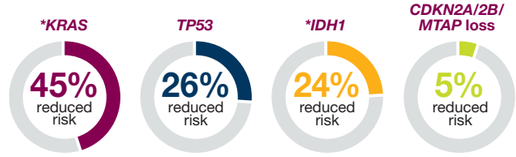
Figure 4. Percentage of participants in Asia or the rest of the world with alterations



*Clinically actionable alterations.

- Participants with alterations in *KRAS*, *TP53*, *IDH1*, and *CDKN2A/2B/MTAP* loss had a reduced risk of death after treatment with durvalumab plus chemotherapy versus placebo plus chemotherapy (Figure 5)

Figure 5. Alterations and the reduced risk of death with durvalumab plus chemotherapy versus placebo plus chemotherapy



The number of participants with these alterations was small, and this analysis was exploratory in nature.
*Clinically actionable alterations.

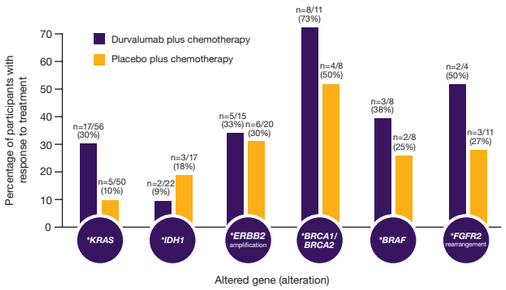
- Participants with alterations in *KRAS*, *TP53*, and *CDKN2A/2B/MTAP* loss had a reduced risk of cancer growth, spread, or worsening after treatment with durvalumab plus chemotherapy versus placebo plus chemotherapy (Figure 6)

Figure 6. Alterations and the reduced risk of cancer growth, spread, or worsening with durvalumab plus chemotherapy versus placebo plus chemotherapy

Alterations associated with an increased risk of cancer growth, spread, or worsening with durvalumab plus chemotherapy versus placebo plus chemotherapy (*ARID1A*, *IDH1*, and *ERBB2* amplification) are not shown. The number of participants with these alterations was small, and this analysis was exploratory in nature.
*Clinically actionable alterations.

- In general, more participants whose tumours had clinically actionable alterations who took durvalumab plus chemotherapy had their cancer shrink or disappear after treatment than those who took placebo plus chemotherapy (Figure 7)

Figure 7. Percentage of participants who had their cancer shrink or disappear after treatment



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Disclosures

VG, PM, YSL, NR, and GC are employees and shareholders in AstraZeneca. MŻ is an employee of AstraZeneca. JWV and D-YO received grant or research support from AstraZeneca. JWV, LA, DT, MI, and D-YO received consulting or advisory fees from AstraZeneca. MI received honoraria from AstraZeneca. SQ, C-kL, and BT have no AstraZeneca-related conflicts of interests to declare.

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