# Immune-mediated adverse event incidence, timing, and association with efficacy in the Phase 3 TOPAZ-1 study of durvalumab or placebo plus gemcitabine and cisplatin in advanced biliary tract cancer

Juan W. Valle,[1] Lorenzo Antonuzzo,[2] Hidenori Takahashi,[3] Joon Oh Park,[4] Aumkhae Sookprasert,[5] Roopinder Gillmore,[6] Sheng-Shun Yang,[7] Juan Cundom,[8] Mila Petrova,[9] Gina Vaccaro,[10] Marielle Holmblad,[11] Julia Xiong,[12] Hyosung Kim,[13] Katrin Heider,[14] Nana Rokutanda,[11] Do-Youn Oh[15]

[1]University of Manchester and the Christie NHS Foundation Trust, Manchester, UK; [2]Clinical Oncology Unit, Careggi University Hospital, and Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy; [3]Department of Gastroenterological Surgery, Osaka International Cancer Institute, Osaka, Japan; [4]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea; [5]Medical Oncology Unit, Department of Medicine, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand; [6]Department of Medical Oncology, Royal Free Hospital, London, UK; [7]Division of Gastroenterology & Hepatology, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan; [8]Instituto de Investigaciones Metabólicas, Buenos Aires, Argentina; [9]Department of Medical Oncology, MHAT Nadezhda, Sofia, Bulgaria; [10]Providence Cancer Institute, Portland, OR, USA; [11]AstraZeneca, Gaithersburg, MD, USA; [12]AstraZeneca, Waltham, MA, USA; [13]AstraZeneca, Osaka, Japan; [14]AstraZeneca, Cambridge, UK; [15]Division of Medical Oncology, Department of Internal Medicine, Seoul National University Hospital, and Cancer Research Institute, Seoul National University College of Medicine, Seoul, South Korea

## Summary

### What is this poster about?

The Phase 3 TOPAZ-1 clinical study looked at treatment with durvalumab (a type of immunotherapy) combined with gemcitabine and cisplatin (chemotherapy) for people with advanced biliary tract cancer (BTC). TOPAZ-1 showed that participants with advanced BTC who were treated with durvalumab plus chemotherapy lived longer than those who were treated with placebo (a dummy drug with no active ingredient) plus chemotherapy. The purpose of this poster was to summarise the side effects associated with the immune system in the TOPAZ-1 study, how often they occurred, their timing in relation to treatment, and if they were associated with the length of time participants with BTC remained alive after being treated with durvalumab plus chemotherapy

### What were the results of the study?

Side effects associated with the immune system were mild and manageable. The timing of side effects associated with the immune system varied. Participants benefited from treatment with durvalumab plus chemotherapy, regardless of whether or not they experienced side effects associated with the immune system

### What do the results of the study mean?

This research, alongside other research from the TOPAZ-1 study, continues to support durvalumab plus chemotherapy as a standard first treatment for people with advanced BTC

### 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 data poster of TOPAZ-1 side effects associated with the immune system can be found here:
https://oncologypro.esmo.org/meeting-resources/esmo-congress/immune-mediated-adverse-event-imae-incidence-timing-and-association-with-efficacy-in-the-phase-iii-topaz-1-study-of-durvalumab-d-or-placebo-p

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Poster



Data in this poster was previously presented at the European Society for Medical Oncology (ESMO) Congress 2022, "FPN (Final Publication Number):57P", "Antonuzzo, et al." - Reused with permission
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Corresponding author email address: juan.valle@nhs.net

## What is the TOPAZ-1 study?

- BTC includes cancer of the bile ducts or gallbladder. People with BTC that cannot be treated with 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
- Durvalumab stimulates the immune system to attack cancer cells and may cause side effects associated with the immune system. Some studies have reported that these types of side effects can be associated with people on immunotherapies living longer
- The purpose of this analysis was to assess side effects associated with the immune system in the TOPAZ-1 study, how often they occurred, their timing in relation to treatment, and if they were associated with the length of time participants with BTC remained alive after being treated with durvalumab plus chemotherapy therapy

## How was the TOPAZ-1 study carried out?

- TOPAZ-1 is a Phase 3 clinical study that included participants from all over the world (Figure 1)
- In the TOPAZ-1 study, participants with BTC not suitable for surgery received either durvalumab or placebo in combination with chemotherapy treatment (Figure 2)
- Side effects associated with the immune system are defined as side effects known to have happened in other studies of immunotherapies, considered to be related to the treatment being studied, and likely associated with the immune system with no other clear cause

**Figure 1. Map of countries and regions where participants were included in the TOPAZ-1 study**

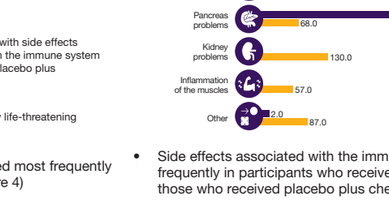


**Figure 2. How the TOPAZ-1 study was carried out**

**Who was included in the study?**

Participants with BTC (cholangiocarcinoma and gallbladder cancer) not suitable for surgery

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

**685** participants were included in the study and randomly assigned to either treatment group

**341** participants were included in the **durvalumab plus chemotherapy** group

**344** participants were included in the **placebo plus chemotherapy** group

**What treatment did participants get?**

A placebo does not contain any medicine, but it looks the same, and is given in the same way, as the treatment being tested (durvalumab). In the study, both the participants and their doctors did not know if the participant received durvalumab or placebo plus chemotherapy. This was done to make sure that any differences measured between the two groups of participants were caused by the treatment only

**What was measured in the study?**

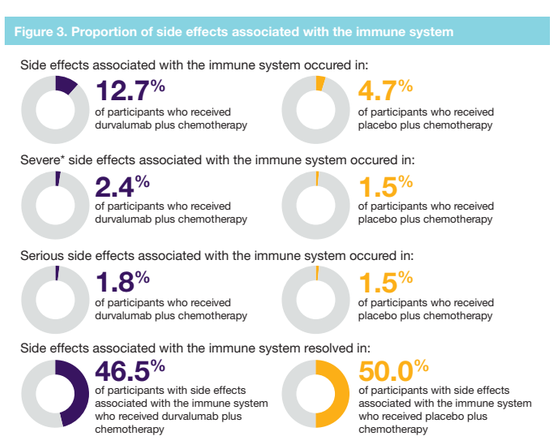
- **The reduction in the risk of death for participants taking treatment**
- **The length of time participants were alive after the start of treatment**
- **The length of time participants had no tumour growth after the start of treatment**
- **The percentage of participants whose cancer shrank or disappeared after treatment**
- **The safety of the treatment**
  - Side effects associated with the immune system

## What were the results of this analysis?

### Side effects associated with the immune system

- Side effects associated with the immune system occurred in more participants who received durvalumab plus chemotherapy than those who received placebo plus chemotherapy (Figure 3)
- There were few severe or serious side effects associated with the immune system in participants receiving either treatment (Figure 3)
- Among participants with side effects associated with the immune system, these side effects resolved in 46.5% of those who received durvalumab plus chemotherapy and 50.0% of those who received placebo plus chemotherapy (Figure 3)

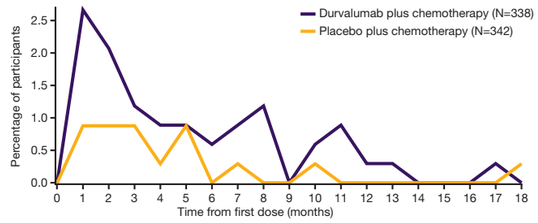
**Figure 3. Proportion of side effects associated with the immune system**




*Severe side effects are defined as severe or medically significant (Grade 3) or potentially life-threatening (Grade 4) side effects

- Overall, side effects associated with the immune system occurred most frequently within 3 months but could occur anytime during treatment (Figure 4)

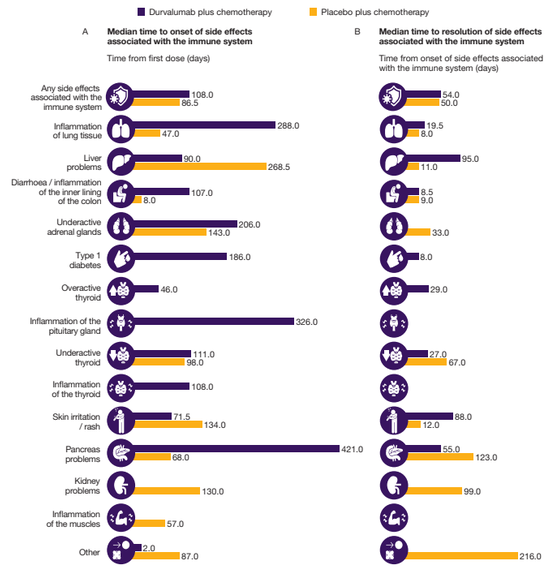
**Figure 4. Percentage of participants with side effects associated with the immune system over time**




- The most common side effects associated with the immune system in participants receiving either treatment were underactive thyroid, skin irritation / rash, liver problems, and underactive adrenal glands (Figure 5)
- In participants who received durvalumab plus chemotherapy, side effects associated with the immune system started a median of 2 to >400 days after first dose. It seems skin irritation / rash usually occurred early on in treatment and inflammation of the lung tissue and some problems relating to glands that produce hormones occurred later on in treatment, although there were only a few participants to compare (Figure 5)

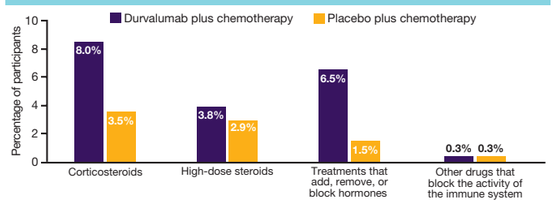
- For the most common types of side effects associated with the immune system that resolved, median time to resolution was less than 100 days (Figure 5)

**Figure 5. Time to onset (A) and resolution (B) of side effects associated with the immune system**




- Side effects associated with the immune system required treatment more frequently in participants who received durvalumab plus chemotherapy than in those who received placebo plus chemotherapy (Figure 6)
- Side effects associated with the immune system were generally manageable and similar to the known side effects of durvalumab

**Figure 6. Treatment of side effects associated with the immune system**

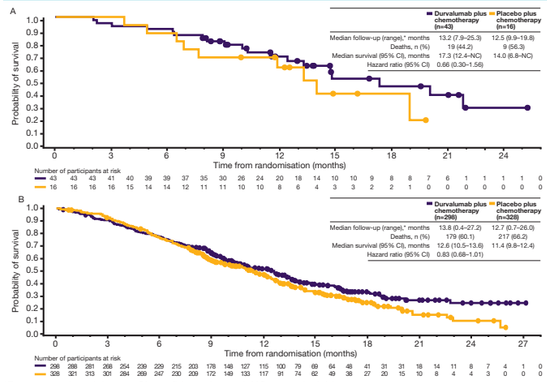



### Overall survival by occurrence of side effects associated with the immune system

- Median duration of follow-up was similar for participants who experienced side effects associated with the immune system versus those who did not in participants receiving either treatment (Figure 7)
- It seems that survival was not shorter in participants who had side effects associated with the immune system compared to those who did not, although there were only a few participants to compare (Figure 7)

- Adding durvalumab to chemotherapy improved survival (shown by a hazard ratio of <1) versus just chemotherapy (placebo plus chemotherapy), regardless of whether participants had side effects associated with the immune system or not (Figure 7)

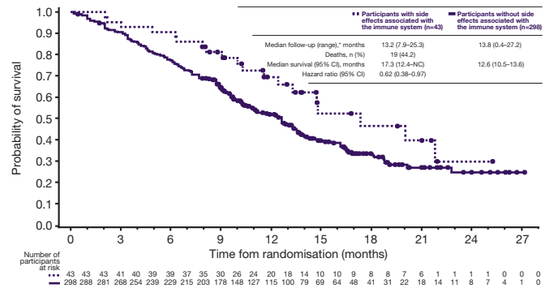
**Figure 7. Overall survival for durvalumab versus placebo for participants with (A) or without (B) side effects associated with the immune system**




*For censored participants. CI, confidence interval; NC, not calculable.

- In participants who received durvalumab plus chemotherapy, those who had a side effect associated with the immune system lived longer than those who did not, confirmed with a hazard ratio of <1 (Figure 8)

**Figure 8. Overall survival by occurrence of side effects associated with the immune system in participants who received durvalumab and chemotherapy**




*For censored participants. CI, confidence interval; NC, not calculable.

## Disclosures

JWV received grant or research support and consulting or advisory fees from AstraZeneca. MH, JX*, HK, KH, and NR are employees of and hold stock in AstraZeneca. LA and D-YO report membership on an advisory board for AstraZeneca. D-YO and HT report research grants from AstraZeneca. LA, AS, JC, and MP report invited speaker roles for AstraZeneca. MP is a principal investigator for AstraZeneca (non-financial). RG, S-SY, JOP, and GV report no conflicts of interest related to AstraZeneca. Full author disclosures are available with the published abstract.

*At the time the study was conducted.

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