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Original Research

Primary results of STRONG: An open-label, multicenter, phase 3b study of fixed-dose durvalumab monotherapy in previously treated patients with urinary tract carcinoma

Guru P. Sonpavde [a,*], Cora N. Sternberg [b,c], Yohann Loriot [d], Aurelien Marabelle [d], Jae Lyun Lee [e], Aude Fléchon [f], Guilhem Roubaud [g], Damien Pouessel [h], Vittorina Zagonel [i], Fabio Calabro [j], Giuseppe L. Banna [k], Sang Joon Shin [l], Francisco E. Vera-Badillo [m], Thomas Powles [n], Eva Hellmis [o], Paulo A.P. Miranda [p], Ana Rita Lima [p], Ugochi Emeribe [q], Sun Min Oh [p], Sebastien J. Hotte [r]

[a] *Medical Oncology, Dana Farber Cancer Institute, 450 Brookline Avenue, Boston, MA 02215, USA*
[b] *Englander Institute for Precision Medicine, Weill Cornell Medicine, Division of Hematology and Oncology, Sandra and Edward Meyer Cancer Center, Hematology/Oncology, 413 E 69th Street, Belfer Research Building, New York, NY 10021, USA*
[c] *Presbyterian Hospital, 1305 York Avenue, New York, NY 10021, USA*
[d] *Department of Cancer Medicine, Gustave Roussy, Université Paris-Saclay, Villejuif, France*
[e] *Department of Oncology and Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-Ro 43-Gil, Songpa-Gu, Seoul 05505, South Korea*
[f] *Department of Medical Oncology, Centre Léon-Bérard, 28 Rue Laennec, 69008 Lyon, France*
[g] *Medical Oncology, Institut Bergonié, 229 Cours de l'Argonne, 33000 Bordeaux, France*
[h] *Medical Oncology Department, Institut Claudius Régaud, IUCT Oncopole, 1 avenue Irène Joliot-Curie, 31059 Toulouse Cedex 9, Toulouse, France*
[i] *Oncology Department, Oncology Unit 1, Veneto Institute of Oncology, IOV, IRCCS, Padua, Italy*
[j] *Medical Oncology, San Camillo Forlanini Hospital, 75 Circonvallazione Gianicolense, 00152 Rome RM, Italy*
[k] [1] *Department of Oncology, Ospedale Cannizzaro, 95126 Catania, Province of Catania, Italy*
[l] *Department of Internal Medicine, Yonsei University Health System, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea*
[m] *Department of Oncology, Queen's University, 25 King St W, K7L 5P9, Kingston, Ontario, Canada*
[n] *Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, Mile End Road, London E1 4NS, UK*

* *Corresponding author:* Medical Oncology, Bladder Cancer Director, Dana Farber Cancer Institute, Faculty, Harvard Medical School, 450 Brookline Avenue, D-924, Boston, MA 02215, USA. Fax: +1 617 632-2165.

E-mail address: guruP_Sonpavde@dfci.harvard.edu (G.P. Sonpavde), cns9006@med.cornell.edu (C.N. Sternberg), Yohann.LORIOT@gustaveroussy.fr (Y. Loriot), aurelien.marabelle@gustaveroussy.fr (A. Marabelle), jaelyun@amc.seoul.kr (J.L. Lee), aude.flechon@lyon.unicancer.fr (A. Fléchon), G.Roubaud@bordeaux.unicancer.fr (G. Roubaud), Pouessel.Damien@iuct-oncopole.fr (D. Pouessel), vittorina.zagonel@iov.veneto.it (V. Zagonel), fcalabro@scamilloforlanini.rm.it (F. Calabro), giuseppe.banna@nhs.net (G.L. Banna), SSJ338@yuhs.ac (S. J. Shin), samantha.biesick@kingstonhsc.ca (F.E. Vera-Badillo), Thomas.Powles@bartshealth.nhs.uk (T. Powles), hellmis@urologicum-duisburg.de (E. Hellmis), paulo.miranda@astrazeneca.com (P.A.P. Miranda), anarita.dantasdelima@astrazeneca.com (A.R. Lima), ugochi.emeribe@astrazeneca.com (U. Emeribe), sunmin.oh@astrazeneca.com (S.M. Oh), hotte@HHSC.CA (S.J. Hotte).

@sonpavde (G.P. Sonpavde)

[1] Affiliation at the time of the study; now at Department of Oncology, Portsmouth Hospitals University NHS Trust, Portsmouth, UK.

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[o] Institut Urologicum Duisburg, Kometenplatz 29-33, 47179, Duisburg, Germany
[p] Oncology Business Unit (OBU), Global Medical Affairs, AstraZeneca, 1 MedImmune Way, Gaithersburg, MD 20878, USA
[q] Statistical Science Immuno-Oncology, AstraZeneca, 1 MedImmune Way, Gaithersburg, MD 20878, USA
[r] Department of Oncology, Juravinski Cancer Centre (JCC), Hamilton Health Sciences 699 Concession Street, Hamilton, ON, Canada

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Immune-related adverse events;
Overall survival;
PD-L1;
Urinary tract carcinoma;
Urothelial carcinoma

Abstract ***Background:*** Prior durvalumab (anti-PD-L1 agent) studies in platinum-refractory metastatic urothelial carcinoma evaluated a dose of 10 mg/kg administered every two weeks. The nonrandomised phase 3b STRONG study (NCT03084471) evaluated the safety and efficacy of fixed-dose durvalumab at a more convenient dosing schedule in a previously treated patient population, more similar to a real-world clinical setting.
Patients and methods: 867 patients with urothelial or nonurothelial urinary tract carcinoma (UTC) who progressed on or after platinum or nonplatinum chemotherapy were treated with durvalumab 1500 mg every four weeks; 87% had an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0–1, and 13% had an ECOG PS of 2. The primary end-point was the incidence of adverse events of special interest (AESIs), including immune-mediated AEs (imAEs). Secondary and exploratory end-points included overall survival (OS), objective response rate (ORR) and disease control rate (at six and 12 months) (DCR).
Results: AESIs of any grade were reported in 51% of patients (8% grade $\geq$ 3). The incidence of imAEs was 11% (2% grade $\geq$ 3). The median OS was 7.0 months (95% confidence interval [CI]: 6.4–8.2) and ORR was 18% (95% CI: 14.8–20.6), with complete responses in 5% of patients and a DCR at six months of 19% (95% CI: 16.1–22.1).
Conclusion: Fixed-dose durvalumab monotherapy every four weeks has an acceptable safety profile and yields durable clinical activity in previously chemotherapy-treated patients with UTC. Safety and efficacy are consistent with previous durvalumab studies and other anti-PD-1/PD-L1 agents in this setting.
Clinicaltrials.gov identifier: NCT03084471 https://clinicaltrials.gov/ct2/show/NCT03084471.

1. Introduction

Patients with advanced urinary tract carcinoma (UTC) failing first-line platinum-based chemotherapy have a poor prognosis [1]. Several immune checkpoint inhibitors (ICIs; antiprogrammed death-ligand 1 (PD-L1) and antiprogrammed death-1 agents) have been studied for the treatment of metastatic urothelial carcinoma (mUC) after progression on platinum-based chemotherapy, which led to their conditional or full approval by the US Food and Drug Administration (FDA) [2–5].

Safety and efficacy of durvalumab 10 mg/kg every two weeks (Q2W) was first assessed in 201 patients with mUC after progression on platinum-based chemotherapy in the phase 1/2, open-label Study 1108 [6–8]. Following pharmacokinetic and pharmacodynamic modelling, a more convenient, fixed-dose, every four weeks (Q4W) schedule was evaluated in other tumor types and granted accelerated approval by the FDA, since re-evaluated based on the outcome of the DANUBE study [9]. Durvalumab was also approved by the FDA and the European Medicines Agency for non-small and small-cell lung cancer [10,11].

The phase 3b STRONG study (NCT03084471) was originally designed to complement phase 3 pivotal trials of durvalumab in solid tumors by further exploring its fixed-dose safety profile. Specifically, the STRONG study evaluated the safety and efficacy of fixed-dose durvalumab (1500 mg Q4W) in 867 patients with urothelial or nonurothelial UTC who progressed on or after platinum or nonplatinum chemotherapy; it was conducted in a population more similar to a real-world clinical setting.

2. Methods

2.1. Study design

STRONG had a modular design in which module A was the UTC-related component (Supplementary Fig. 1). Other STRONG modules including durvalumab plus tremelimumab were originally planned, however, only

module A was opened. A data-monitoring committee reviewed cumulative safety data at regular intervals. It was conducted in accordance with Good Clinical Practice guidelines (International Conference on Harmonisation with provisions of the Declaration of Helsinki). The Clinical Study Protocol and Informed Consent Form were approved by Independent Ethics Committees/Institutional Review Boards. All provided informed written consent.

2.2. Setting and participants

Eligible patients were aged ≥ 18 years and had urothelial or nonurothelial carcinoma of the urinary tract (including urinary bladder, ureter, urethra and renal pelvis). Patients who progressed during or after ≥ 1 platinum/nonplatinum-based chemotherapy for metastatic disease and those who received only prior perioperative chemotherapy progressed < 12 months after adjuvant or neoadjuvant chemotherapy were eligible. An Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0–2 and a creatinine clearance > 40 mL/min were also required. Exclusions included other malignancy within five years or concurrent chemotherapy, investigational agent, biologic or hormonal cancer therapy, investigational or anticancer therapy within 28 days. (For additional inclusion and exclusion criteria, see Supplementary Information: study protocol).

2.3. Intervention(s)

Durvalumab 1500 mg Q4W was administered intravenously until progressive disease, unacceptable toxicities or consent withdrawal. Treatment continued if patients received clinical benefit in the investigator's opinion, unless any discontinuation criteria were met (Supplementary Information: study protocol). Safety follow-up occurred 90 days after the last dose and survival follow-ups occurred every three months until final data cut-off (Supplementary Fig. 1).

A complementary diagnostic assay for PD-L1 was developed, though this assessment was not required for durvalumab use in the second-line setting [12]. In STRONG, PD-L1 expression evaluation required patient consent but was not mandatory. The VENTANA PD-L1 (SP263) Assay (Ventana Medical Systems, Tucson, AZ, USA) was used to determine tumor PD-L1 expression [13,14]. High PD-L1 expression was defined as ≥ 25% of tumor cells with membrane staining or ≥ 25% of immune cells staining for PD-L1 at any intensity.

2.4. Outcome measurements

The primary end-point was incidence of adverse events (AEs) of special interest (AESIs) (including immune-mediated AEs [imAEs]). AESIs previously observed with durvalumab can be found in Supplementary Table 1. AESIs included events with a potential inflammatory or immune-mediated mechanism requiring interventions such as steroids, immunosuppressants and/or hormone replacement therapy. An imAE was an event associated with drug exposure and consistent with an immune-mediated mechanism of action but no clear alternate etiology. In addition to standard AESI assessment, a programmatic-identification algorithm was used to identify imAEs by reviewing AESIs and AEs of potential interest (AEPI [AESIs not considered to have an inflammatory etiology or immune-mediated mechanism]). The algorithm considered interventions involving systemic steroid therapy, immunosuppressant use and/or endocrine therapy (standard endocrine supplementation and symptom treatment resulting from endocrine disorders, i.e. β-blockers for hyperthyroidism). Independent from the severity of the AE, if an investigator considered any given AE was a suspected imAE, these would follow the algorithm (even if not in the Preferred Term AESI list) and only if concomitant medication(s) of interest was/were used would they be identified as imAEs. If the AE was not described as an AESI or AEPI and, cumulatively, was not labelled by the investigator as a suspected imAE and there was no concomitant medication—including steroids and/or endocrine therapy and/or immunosuppressants—the AE was not captured by the automated identification process. AEPIs occurred after first considering investigator-assessed causality and/or an investigator's designation of an event being immune-mediated (Fig. 1). AEs with an onset date on or after the first dose date and ≤ 90 days after treatment discontinuation, were recorded.

Secondary end-points included the incidence of treatment-related AEs (TRAEs), including serious AEs (SAEs), and overall survival (OS), defined as from study entry until death from any cause. OS rates at one and two years were also calculated. Exploratory end-points included objective response rate (ORR), and disease control rate (DCR) based on investigator-assessed response to treatment (Response Evaluation Criteria in Solid Tumors [RECIST] v1.1 was recommended but not required). DCR at six and 12 months was defined as the percentage of patients who had a best overall response of complete or partial response (CR or PR) or stable disease (without subsequent cancer therapy) for ≥ 5 or 11 months, respectively, following treatment start.

2.5. Statistical analysis

As STRONG was designed as a safety study, no formal sample size calculation was planned or performed. While the exact sample size and AESI incidence rate was unknown *a priori*, up to 867 patients were required to provide no more than ± 2% precision with a true AESI incidence of < 5%. The primary statistical analysis was descriptive. OS was calculated using the Kaplan–Meier method with median OS and associated 95% confidence interval (CI)

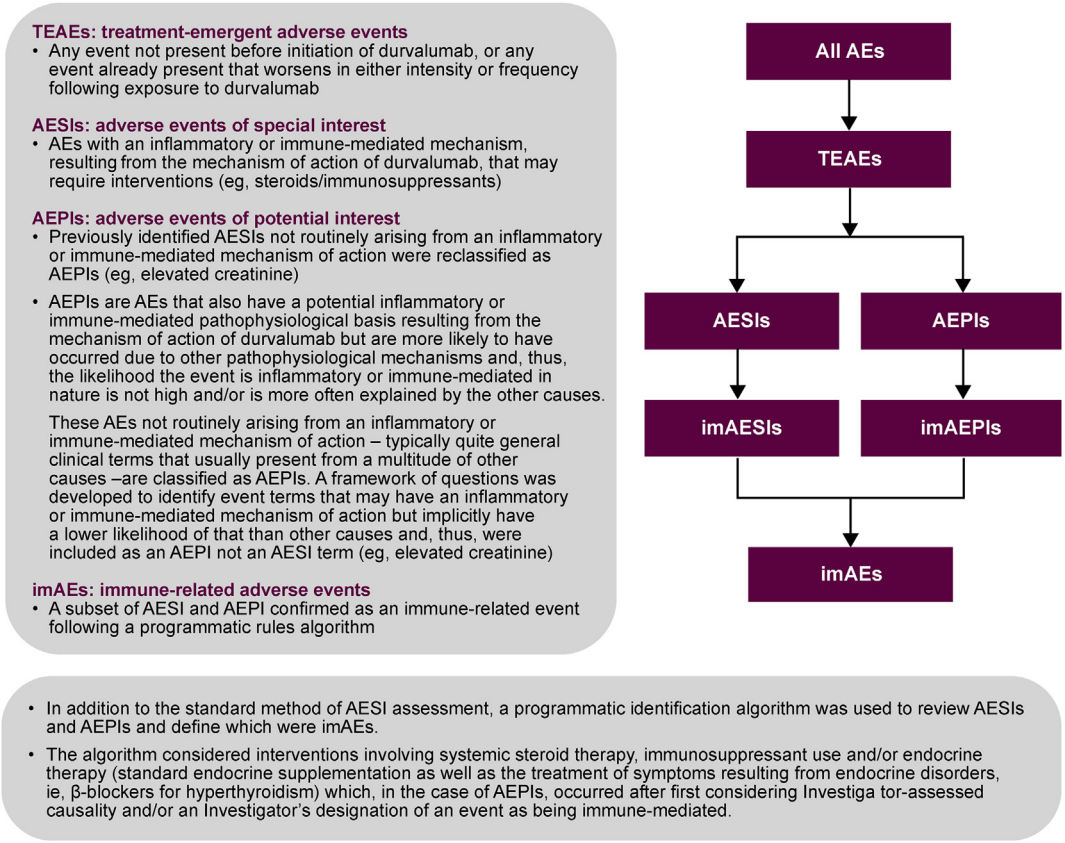

Fig. 1. **Data flow using the imAE programmatic identification algorithm**. AE, adverse event; AEPI, adverse event of potential interest; AESI, adverse event of special interest; imAE, immune-mediated adverse event.

reported, plus the proportion of patients alive up to two years. ORR and DCR were reported as *n* (%) with associated 95% CI. OS subgroup analyses were conducted *post hoc* (Supplementary Information: statistical analysis plan).

3. Results

STRONG began in April 2017 but enrollment was halted in August 2019 as the sample size required to characterise the incidence of AESIs adequately was met; data cut-off was March 31, 2020. Eight hundred sixty seven patients received durvalumab (Fig. 2) at 77 sites in 8 countries. Median age was 68.1 years, 80% were male, 87% had an ECOG PS of 0–1, for 13% it was 2 (Table 1). Most (88%) had urothelial carcinoma. Of the 577 patients with PD-L1 expression available, tumor PD-L1 expression was high in 239 (41%). At data cut-off, median treatment duration was 12.1 weeks (range: 1–128) and 31% were being followed for survival; median follow-up was 13.8 months (range: 0–29).

3.1. Safety

AEs of any grade occurred in 787 patients (91%) (Table 2; Supplementary Fig. 2), the most common being asthenia (27%), constipation (20%), anemia (21%), decreased appetite (17%) and diarrhea (16%). In 47% of patients receiving durvalumab (n = 407), the investigator considered AEs to be TRAEs. Grade ≥ 3 AEs occurred in 365 (42%) patients receiving durvalumab and were considered TRAEs in 78 (9%). SAEs occurred in 254 (29%) patients receiving durvalumab, and 41 (5%) of SAEs were designated as TRAEs (Table 2; Supplementary Fig. 2).

AESIs of any grade were reported in 438 patients (51%); 8% were grade ≥ 3 (Table 2; Supplementary Fig. 2). Median duration of AESIs was 141.5 days (range: 1–855); median time to AESI resolution was 84.5 days (range: 1–892). Using the programmatic identification algorithm (Fig. 1), AESIs of any grade were reported in 265 patients (31%); 2% were grade ≥ 3. AESIs recorded in all patients receiving durvalumab included diarrhea/colitis (n = 146; 17%), dermatitis/rash (n = 87; 10%), hypothyroid events (n = 57; 7%), hyperthyroid events (n = 43; 5%) and hepatic events (n = 6; 1%). AESIs of grade ≥ 3 reported were diarrhea/colitis (n = 13; 2%), dermatitis/rash (n = 5; 1%) and hepatic events (n = 2; 0.2%) (Table 3). imAEs of any grade were reported in 97 patients (11%; of which 2% were grade ≥ 3) (Table 2). The most common imAEs were hypothyroid events (n = 46; 5%), dermatitis/rash (n = 16; 2%), diarrhea/colitis (n = 14; 2%), hyperthyroid events (n = 10; 1%), hepatic (n = 5; 1%) and renal events (n = 1; 0.1%). Grade ≥ 3 imAEs reported were diarrhea/

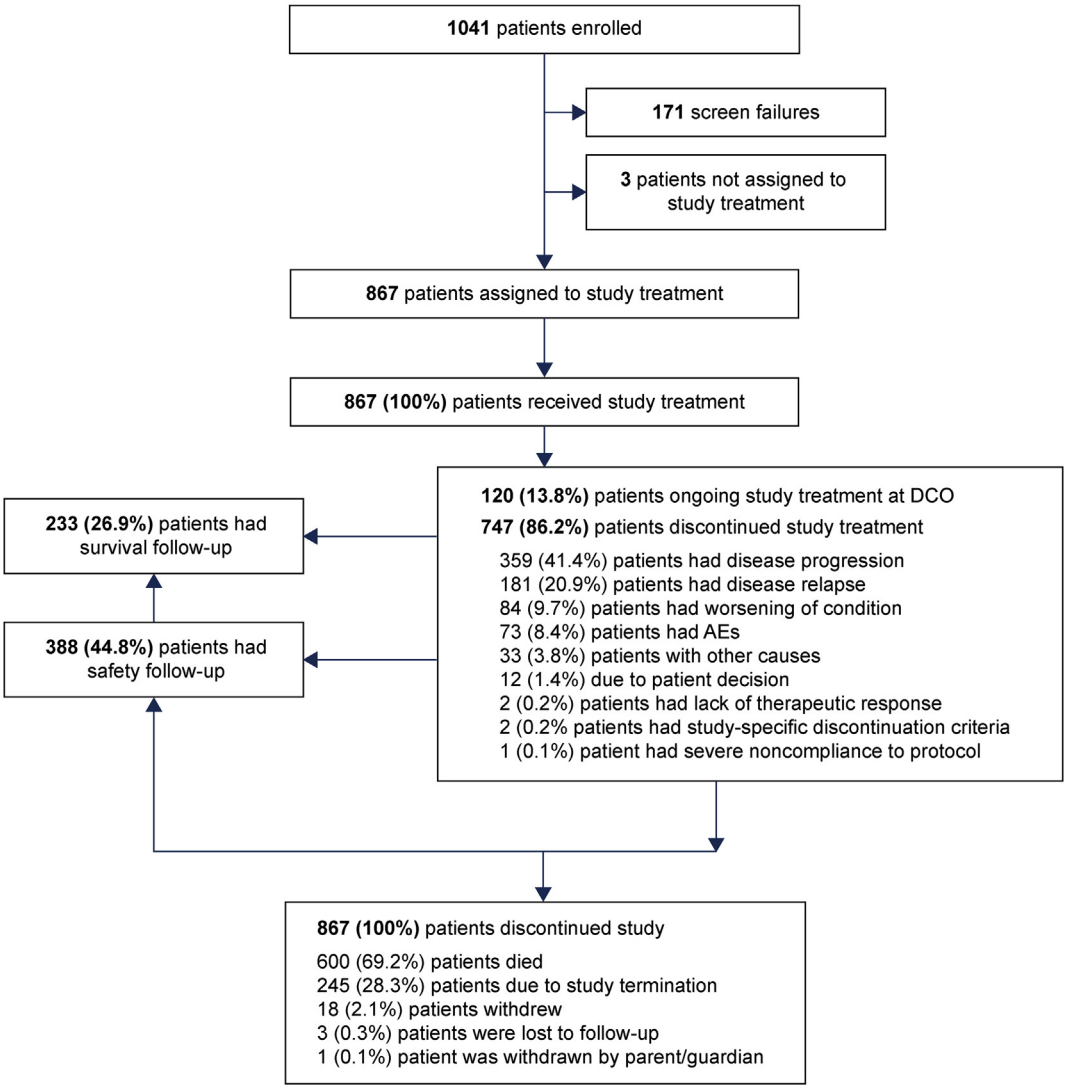

Fig. 2. **STRONG module A patient disposition**. AE, adverse event; DCO, data cut off.

colitis (n = 7; 1%), dermatitis/rash (n = 3; 0.3%), hepatic (n = 4; 1%), and renal events (n = 1; 0.1%) (Table 3). The median time to onset of imAEs was 85 days (range: 1–515). Of those experiencing an imAE, 48 (6%) were treated with systemic corticosteroids and 25 (3%) with high-dose steroids (defined as ≥ 40 mg prednisone or equivalent per day). 1 patient (0.1%) was given infliximab and vedolizumab for colitis. Endocrine therapy was administered to 61 (6%) patients with imAEs; 60 (6%) were treated with endocrine supplementation or for symptoms of endocrine disease; 1 (0.1%) with insulin (for hyperglycemia in type 1 diabetes). Median time to initiation of first steroid dose for imAE treatment and time to high-dose steroid was 6.5 (range: 0–293) and 9.5 days (range: 0–293), respectively.

The total number of deaths for any reason was 600 (69%); deaths at 30, 60 and 90 days, and by ECOG PS are included in Supplementary Table 2. Deaths due to a TRAE occurred in 9 patients (1%). It was determined that none of the 9 fatal TRAEs were imAEs.

3.2. Efficacy

Median OS was 7.0 months (95% CI: 6.4–8.2). OS rates at one and two years were 35.8% (33–39%) and 20% (17–24%), respectively (Supplementary Table 3; Fig. 3). Patients with high and low PD-L1 expression had a median OS of 9.3 (n = 239; 95% CI: 6.7–12.7) and 6.5 months (n = 338; 95% CI: 5.8–8.1). The median OS of those with an ECOG PS of 0–1 or 2 was 8.4 (95% CI: 7.2–9.8) and 3.0 months (95% CI: 2.0–4.1). Patients with lymph node-only disease had a median OS of 12.0 (95% CI: 7.5–16.1), compared with 8.1 (95% CI: 6.9–9.3) for patients with extrahepatic visceral metastases and 3.3 months (95% CI: 2.8–4.1) for patients with liver metastases (Supplementary Table 3; Fig. 3). OS outcomes in other subgroups, including primary tumor location, prior chemotherapy, histology, age and tumor stage, are summarised in Supplementary Table 3 and Supplementary Fig. 3.

Table 1
Baseline patient characteristics.

Characteristic		$N = 867$
Median age, (range) years		68.1 (21–89)
Sex, *n* (%)	Male	694 (80)
	Female	173 (20)
Race,[a] *n* (%)	White	508 (84)
	Asian	65 (11)
	Black or African American	2 (0.3)
	Other	28 (5)
ECOG PS, *n* (%)	0	350 (40)
	1	405 (47)
	2	110 (13)
	3	2 (0.2)
AJCC stage at baseline, *n* (%)	Stage III	79 (9)
	Stage IV	781 (90)
Tumor primary location, *n* (%)	Lower tract	659 (76)
	Upper tract	196 (23)
	Other[b]	12 (1)
Sites of disease at baseline, *n* (%)	Liver (+/− other metastases)	146 (17)
	Lymph node only	102 (12)
	Nonliver visceral metastases	619 (71)
Histology, *n* (%)[c]	Urothelial (TCC, nonvariants)	766 (88)
	Urothelial (TCC, variants)	68 (8)
	Nonurothelial[d]	32 (4)
PD-L1 expression status, *n* (%)	High	239 (28)
	Low/negative	338 (39)
	Unknown	290 (33)
Prior systemic therapy, *n* (%)	1	563 (65)
	2	209 (24)
	3	55 (6)
	≥ 4	33 (4)
	Unknown	7 (1)
Previous therapy with platinum-based regimen, *n* (%)	Platinum	833 (96)
	Nonplatinum	34 (4)
	Cisplatin	416 (48)
	Carboplatin	289 (33)
	Cisplatin and carboplatin	128 (15)
Lactate dehydrogenase	Low	414 (48)
	Normal	254 (29)
	>1 × ULN to 2 × ULN	43 (5)
	>2 × ULN	7 (1)
	Unknown	149 (17)

AJCC, American Joint Committee on Cancer; ECOG PS, Eastern Cooperative Oncology Group performance status; PD-L1, programmed death ligand 1; TCC, transitional cell carcinoma; ULN, upper limit of normal.

[a] Race was collected for 603 patients only as race was not allowed to be recorded in all countries.

[b] Categorized by investigators as urothelium, bladder and ureter, bone (left ischiopubic ramus), UC of the bladder and intramural ureter on the right and UC on adrenal metastases.

[c] Histology classification was missing in 1 patient.

[d] Categorized by investigators as adenocarcinoma typical; cannot be determined; squamous cell carcinoma, typical; mixed cell type; undifferentiated carcinoma; adenocarcinoma; variant histology; epidermoid carcinoma; neuroendocrine tumor; poorly differentiated carcinoma with rhabdoid differentiation.

ORR and DCR were assessed in 690 patients for whom RECIST v1.1 data were collected. An ORR of 18% was achieved with CR in 5% of patients and PR in 13% (Supplementary Table 4). Patients with high PD-L1 expression had a higher ORR (28%) than the overall population (18%) (Supplementary Table 4). Overall, DCR at six months was 19% (defined in 239 patients [35%]) but could not be defined for 451 (65%) patients.

4. Discussion

STRONG afforded the opportunity to evaluate durvalumab's safety and efficacy in the Q4W fixed-dosing regimen in a large study of previously treated patients with UTC in several countries and settings, reflecting the real-world clinical experience. Durvalumab was generally well tolerated, and results are consistent with previous experience using 10 mg/kg Q2W and no new safety-related issues identified.

For STRONG, a refined programmatic identification of AEs was developed to reduce the misclassification bias of AESIs and imAEs and provide a more accurate adjudication of AEs (Global imAE Characterization Charter). The charter has been applied to previous and ongoing AstraZeneca-sponsored trials [15–19], and is regularly updated as a result of interactions with regulatory agencies. It is an automated process that allows for imAE frequencies to be calculated from both AESIs and AEPIs based on applied rules and a treatment algorithm that considers interventions involving systemic steroid therapy, immunosuppressant use, and/or endocrine therapy (which, in the case of AEPIs, occurs after first considering an investigator's causality assessment and/or an investigator's designation of an event as immune-mediated). Using the standard approach, AESIs in STRONG occurred in 50% of patients. However, when the programmatic identification algorithm was applied, the incidence of AESIs was 31% with AEPIs at 35%. In Study 1108 of 10 mg/kg Q2W durvalumab in platinum-refractory mUC, 104/191 (55%) patients had ≥ 1 AESI and 66 (35%) had treatment-related AESIs. Programmatically derived AESIs in STRONG, excluding AEPIs, are comparable with the treatment-related AESIs in Study 1108 [6]. Incidence of imAEs were similar in both (STRONG: 11%; 1108: 12%), as was the percentage of patients given systemic steroids to treat imAEs (STRONG: 6%; 1108: 7%) [6]. The incidence of imAEs and frequency of systemic steroid administration may indicate an unmet need for educating patients and clinicians on imAE signs and symptoms and the importance of early and appropriate immunosuppressive therapy intervention.

Median OS in STRONG was seven months. In Study 1108, which included patients with an ECOG PS of 0–1 and those who received ≤ 2 prior lines of systemic therapy, median OS was 11 months [6,8]. The lower median OS reported in STRONG may be explained by more inclusive patient eligibility criteria, such as patients with an ECOG PS of 2, reflecting a population closer to real-world clinical practice. Another all-comer population reflecting real-world experience and patients

Table 2
Safety summary.

	Standard assessment $n = 867$			Programmatic identification algorithm assessment $n = 867$			
	All AEs (%)	TRAEs (%)	AESI (%)	AESI and AEPIs (%)	AESI (%)	AEPIs (%)	imAEs (%)
Any AE	787 (91)	407 (47)	438 (51)	436 (50)[a]	265 (31)	300 (35)	97 (11)
Grade ≥ 3 AEs	365 (42)	78 (9)	69 (8)	68 (8)	21 (2)	49 (6)	17 (2)[b]
Serious AEs	254 (29)	41 (5)	32 (4)	31 (4)	19 (2)	13 (2)	11 (1)
AEs leading to discontinuation of treatment	77 (9)	33 (4)	18 (2)	18 (2)	12 (1)	7 (1)	10 (1)
AEs leading to death	42 (5)	9 (1)	1 (0.1)	1 (0.1)	1 (0.1)	0 (0)	0 (0)

AE, adverse event; AEPI, adverse event of potential interest; AESI, adverse event of special interest; imAE, immune-mediated adverse event; TRAE, treatment-related adverse event.

[a] Infusion-related reactions and hypersensitivity/anaphylactic reactions occur via a mechanism of action different than that for imAEs, and thus were not considered imAEs. These reactions were excluded from the algorithm, accounting for the $n = 2$ fewer patients assessed via the algorithm.

[b] Following the programmatic identification algorithm assessment no grade 5 events were recorded, only grade 3 and 4 imAEs were included.

ineligible for registration trials is the SAUL study, with a median OS of nine months. In the phase 3 registration studies of pembrolizumab (KEYNOTE-045) and atezolizumab (IMvigor211) median OS was not that different; ten and nine months, respectively [20–22]. Survival outcomes of patients with ECOG PS 2 were much worse than those with an ECOG PS of 0–1 (median OS of three months versus 8.4 months), consistent with the SAUL study where median OS for ECOG PS 2 was two months. Patients who have an ECOG PS of 2 may not be well enough to allow the treatment time to take effect in these studies or may reflect even poorer PS at the time of initiation. In future trials, justification for the ECOG PS classification should be taken into consideration, i.e. tumor burden or co-morbidities, to assess the impact on survival. It is recognised that patients with ECOG PS 2 reflect a heterogeneous group and some patients may be healthier and closer to ECOG PS 1 and others less well and closer to ECOG PS 3.

The ORR in STRONG was similar to that reported in Study 1108 (STRONG: 18%; 1108: 17%) [8], which, together with DOR, formed the basis for the FDA's accelerated approval of durvalumab in patients with UTC following platinum-containing chemotherapy in May 2017. As an FDA post-approval requirement of second-line durvalumab, the confirmatory phase 3 DANUBE trial was conducted in the first-line setting. However, DANUBE did not meet either coprimary end-point of improving OS with durvalumab in the PD-L1 high population or durvalumab plus tremelimumab (an anti-cytotoxic T-lymphocyte antigen 4 agent) in the overall population versus standard of care chemotherapy [9]. The outcome of DANUBE, and availability of other fully approved IO therapies in the second-line setting, led to AstraZeneca voluntarily withdrawing the second-line durvalumab indication in the United States in February 2021 [23]. Of note, prespecified secondary analyses in DANUBE suggested greater antitumor activity and prolonged survival with durvalumab plus tremelimumab in the PD-L1-high population compared with all randomised patients [9]. These results emphasise the critical importance of considering study end-points based on robust biostatistical assumptions, known mechanisms of disease and therapeutic agents, plus clinicopathological and molecular characterisation of study populations prior to study initiation.

Table 3
The most common AESIs, AEPIs and imAEs; any grade and grade 3 to 4[a] reported following the programmatic identification algorithm.

	Dermatitis/rash		Diarrhea/colitis		Hepatic events		Hypothyroid events		Renal events		Hyperthyroid events	
	Any grade	Grade 3 to 4	Any grade	Grade 3 to 4	Any grade	Grade 3 to 4	Any grade	Grade 3 to 4	Any grade	Grade 3 to 4	Any grade	Grade 3 to 4
AESI or AEPI, *n* (%)	171 (20)	8 (1)	152 (18)	13 (2)	68 (8)	13 (2)	60 (7)	0	53 (6)	5 (1)	47 (5)	0
AESI, *n* (%)	87 (10)	5 (1)	146 (17)	13 (2)	6 (1)	2 (0.2)	57 (7)	0	0	0	43 (5)	0
AEPI, *n* (%)	119 (14)	3 (0.3)	7 (1)	0	62 (7)	11 (1)	4 (1)	0	53 (6)	5 (0.6)	5 (1)	0
imAE, *n* (%)	16 (2)	3 (0.3)	14 (2)	7 (1)	5 (1)	4 (1)	46 (5)	0	1 (0.1)	1 (0.1)	10 (1)	0

AEPI, adverse event of possible interest; AESI, adverse event of special interest; imAE, immune-mediated adverse event; TRAE, treatment-related adverse event.

[a] Following the programmatic identification algorithm assessment no grade 5 events were recorded, only grade 3 and 4 imAEs were included.

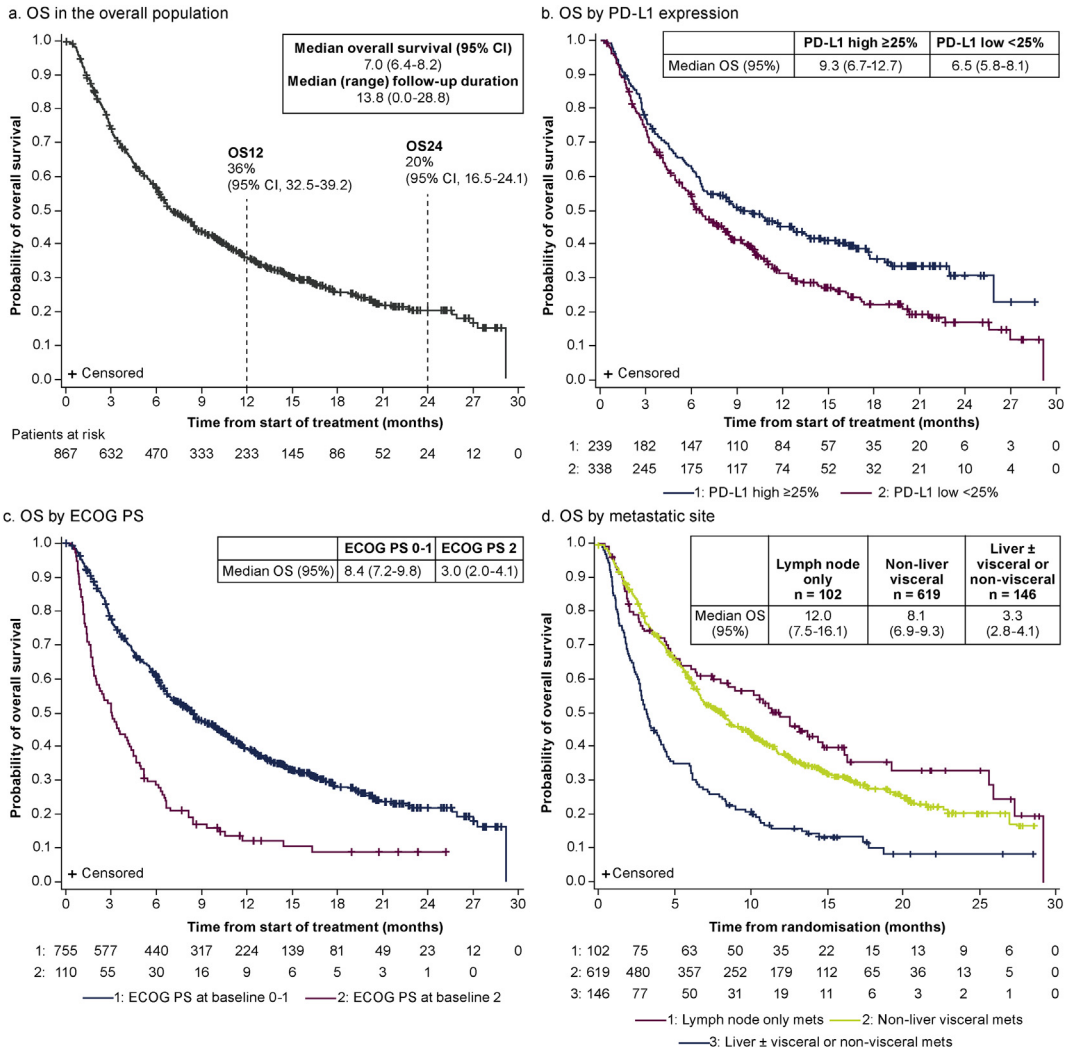

Fig. 3. **OS: overall population and select subgroups**. Analyses of OS for subgroups were conducted post hoc. ECOG PS, Eastern Cooperative Oncology Group performance status; OS, overall survival; PD-L1, antiprogrammed death ligand 1.

Several prognostic factors for higher survival have been identified for ICIs in second-line mUC, including an ECOG PS of 0–1, PD-L1 high-expressing tumors and absence of liver metastases [9,24], but require further investigation in a wider UTC population. Consistent with known factors [9,24], STRONG demonstrated prolonged survival in patients with an ECOG PS of 0–1, high PD-L1 expression, lymph node-only metastases at baseline, prior cisplatin chemotherapy and lower tumor stage at baseline. Further understanding of prognostic and predictive factors in this population, combined with molecular/biomarker profiling may enhance the selection of patients more likely to derive clinical benefit from durvalumab or experience serious and immune-mediated toxicities. An exploratory ancillary biomarker study based on a subset of STRONG patients is currently ongoing [25].

Approval of the durvalumab Q4W fixed-dosed regimen by the FDA was based on data from several durvalumab clinical trials across indications including non-small cell lung cancer and extensive-stage small cell lung cancer [10]. A fixed-dosed treatment regimen improves patient convenience by reducing time required for medical visits, additionally reducing burden on caregivers required to assist visits. Fewer visits also limit potential exposure to infection in the healthcare environment for a population that is especially vulnerable to complications from COVID-19 (STRONG median age 68.1 years). From a healthcare provider perspective, a fixed-dose regimen is easier to prepare than a weight-based regimen and less prone to error and hospital resources can be utilised more efficiently.

STRONG limitations include the single-arm, open-label design. Subgroup categories to assess OS were

determined *post hoc* with low patient numbers in some subgroups. Assessment of tumor response was not standardised and RECIST v1.1 was recommended but not mandatory given the exploratory nature of this end-point and reflective of real-world clinical practice. Consequently, the patient numbers with stable disease may have been underestimated, resulting in a lower DCR.

5. Conclusions

Fixed-dose durvalumab Q4W has an acceptable safety profile in previously treated patients with UTC in a population similar to a real-world setting. Safety data were consistent with published durvalumab and other ICI studies in platinum-refractory disease, with no new safety signals observed. Durvalumab resulted in objective tumor responses consistent with published evidence from clinical trials. Better survival outcomes and a higher number of patients achieving objective responses were observed among those with high PD-L1 expression and an ECOG PS of 0–1.

Data sharing and data accessibility

Data underlying the findings described in this manuscript may be obtained in accordance with AstraZeneca's data sharing policy described at: https://astrazenecagrouptrials.pharmacm.com/ST/Submission/Disclosure.

Author contributions

Guru P. Sonpavde: Conceptualization, Methodology, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing. **Cora N. Sternberg:** Methodology, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing. **Yohann Loriot:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Aurelien Marabelle:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Jae Lyun Lee:** Methodology, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing. **Aude Flechon:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Guilhem Roubaud:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Damien Pouessel:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Vittorina Zagonel:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Fabio Calabro:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Giuseppe L. Banna:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Sang Joon Shin:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Francisco E. Vera-Badillo:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Thomas Powles:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Eva Hellmis:** Investigation, Resources, Data Curation, Writing - Review & Editing. **Paulo A. P. Miranda:** Conceptualization, Methodology, Formal analysis, Writing - Original Draft, Writing - Review & Editing, Project administration. **Ana Rita Lima:** Conceptualization, Validation, Formal analysis, Data Curation, Writing - Original Draft, Writing - Review & Editing, Project administration. **Ugochi Emeribe:** Validation, Formal analysis, Data Curation, Writing - Original Draft, Writing - Review & Editing. **Sun Min Oh:** Formal analysis, Writing - Original Draft, Writing - Review & Editing, Project administration. **Sebastien J. Hotte:** Methodology, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing.

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Conflict of interest statement

The following authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper: Sang Joon Shin and Guilhem Roubaud.

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Appendix A. Supplementary data

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