Safety and efficacy of atezolizumab in patients with autoimmune disease: Subgroup analysis of the SAUL study in locally advanced/metastatic urinary tract carcinoma

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Abstract ***Aim:*** Patients with pre-existing autoimmune disease (AID) are typically excluded from clinical trials of immune checkpoint inhibitors and there are limited data on outcomes in this population. The single-arm international SAUL study of atezolizumab enrolled a broader 'real-world' patient population. We present outcomes in patients with a history of AID.

Methods: Patients with locally advanced/metastatic urinary tract carcinoma received atezolizumab 1200 mg every 3 weeks until loss of clinical benefit or unacceptable toxicity. The primary endpoint was safety. Overall survival (OS) was a secondary endpoint. Subgroup analyses of AID patients were prespecified.

Results: Thirty-five of 997 treated patients had AID at baseline, most commonly psoriasis (*n* = 15). Compared with non-AID patients, AID patients experienced numerically more adverse events (AEs) of special interest (46% vs 30%; grade ≥3 14% vs 6%) and treatment-related grade 3/4 AEs (26% vs 12%), but without relevant increases in treatment-related deaths (0% vs 1%) or AEs necessitating treatment discontinuation (9% vs 6%). Pre-existing AID worsened in six patients (17%; two flares in two patients): four of the eight flares resolved, one was resolving and three were unresolved. Efficacy was similar in AID and non-AID patients (median OS 8.2 vs 8.8 months, respectively; median progression-free survival 4.4 vs 2.2 months; disease control rate 51% vs 39%).

Conclusions: In 35 atezolizumab-treated patients with pre-existing AID, incidences of special-interest and treatment-related AEs appeared acceptable. AEs were manageable, rarely requiring atezolizumab discontinuation. Treating these patients requires caution but pre-existing AID does not preclude atezolizumab therapy.

Trial registration: NCT02928406.

KEYWORDS

Atezolizumab;

Autoimmune disease;

Psoriasis;

Immunotherapy;

Urothelial carcinoma

1. Introduction

In recent years, immunotherapy has transformed the standard of care for several cancers and dramatically improved outcomes for patients who respond to these treatments [1]. Urothelial cancer is no exception. There are now five immunotherapeutic agents targeting programmed cell death-1 (PD-1) or programmed cell death ligand-1 (PD-L1) approved for the treatment of urothelial cancer [2]. The first of these agents to be approved, atezolizumab, is a monoclonal antibody that targets PD-L1 [3,4]. Atezolizumab is approved as treatment for locally advanced or metastatic urothelial cancer in patients who have received prior platinum-containing chemotherapy, or are considered cisplatin ineligible and have PD-L1-positive tumours (PD-L1 expression ≥5%), or are ineligible for any platinum, irrespective of PD-L1 status (US only) [5,6].

Cancer patients with autoimmune disease (AID) represent a particular challenge in clinical practice with regard to treatment with immunotherapeutic agents. Patients with several common AIDs, such as systemic lupus erythematous, rheumatoid arthritis or inflammatory bowel disease, have an increased risk of developing cancer [7–11]. Patients with significant pre-existing AID are usually excluded from clinical trials, as was the case for the IMvigor210 and IMvigor211 trials of atezolizumab [12–16], and there are limited data on outcomes in patients with AID treated with immune checkpoint inhibitors. The risk of immune-related adverse events (AEs) may be increased in patients with AID and consequently there has been hesitancy to treat these patients with cancer immunotherapy [7,17–19].

The international SAUL study (NCT02928406) enrolled patients with locally advanced or metastatic urothelial or non-urothelial carcinoma of the urinary tract more representative of real-world practice, including patients with AID [20]. In this broader population of atezolizumab-treated patients, median overall survival (OS) was 8.7 months (95% confidence interval [CI] 7.8–9.9 months) and the safety profile was consistent with that reported with atezolizumab monotherapy in more selected populations. Here we report

prespecified analyses of safety and efficacy in the subgroup of patients with AID treated in the SAUL study.

2. Patients and methods

The design of the SAUL trial has been described in detail elsewhere [20]. In brief, the study enrolled patients with locally advanced/metastatic urothelial or non-urothelial carcinoma of the urinary tract. Of note, patients were not excluded for any of the following characteristics and conditions: Eastern Cooperative Oncology Group performance status 2; progression on prior non-platinum treatment; creatinine clearance <30 (but ≥15) mL/min; treated asymptomatic central nervous system metastases; ongoing steroid treatment at baseline; HIV-positive status; or stable controlled AID. Patients with a history of AID were eligible if their AID was controlled and they were on stable treatment for the preceding 12 weeks, except for: patients receiving concurrent abatacept (a biological disease-modifying anti-rheumatic drug indicated for psoriatic and rheumatoid arthritis) or belatacept (a selective T-cell costimulation blocker indicated for prophylaxis of renal transplant rejection) treatment, unless therapy had been withdrawn for >8 weeks; patients with a history of serious or life-threatening immune-related AEs; and patients with two or more concomitant AIDs (with specific exceptions, such as controlled type 1 diabetes mellitus or controlled autoimmune-related hypothyroidism). The full list of permitted AIDs is provided in Supplementary Appendix A. All patients provided written informed consent before undergoing any study-specific procedures.

All patients received atezolizumab 1200 mg intravenously every 3 weeks until loss of clinical benefit, unacceptable toxicity, patient or investigator decision to withdraw from therapy or death. If a patient with pre-existing AID experienced a grade 2 or 3 flare of their AID, atezolizumab was interrupted until the patient responded to treatment of the AID and the condition stabilised. If a patient with pre-existing AID experienced a grade 4 flare, atezolizumab was discontinued permanently. In both situations, the patient was to be referred to an appropriate specialist.

The primary endpoint was safety. Secondary endpoints were OS, progression-free survival (PFS), overall response rate, disease control rate and duration of response. Subgroup analyses of patients with versus without AID were prespecified. AEs of special interest represent immune-related AEs predefined based on the mechanism of action of atezolizumab and include potential dermatologic, hepatic, endocrine and respiratory events and autoimmune flares. The full list is provided in Supplementary Appendix Table A1. Worsening AIDs were identified by review of individual AEs.

3. Results

3.1 Patient population and treatment exposure

Between November 2016 and March 2018, 1004 patients were enrolled from 32 countries. Among the 997 treated patients, 35 presented with AID at baseline. The most common pre-existing conditions were psoriasis (*n* = 15), thyroid AID (*n* = 6) and rheumatoid arthritis (*n* = 4) (Fig. 1). Three patients had two AIDs: all three had psoriasis, with concurrent hypothyroidism in two patients and autoimmune thyroiditis in the other. In the majority of cases, AID was ongoing (with or without treatment) at study entry. Two of the 11 patients receiving treatment for active AID at study entry were receiving systemic steroids (Supplementary Appendix Table A2). Baseline characteristics were similar in the AID and non-AID subgroups (Table 1).

At the data cut-off (16 September 2018), patients in the AID subgroup had received a median of nine cycles (range 1–22 cycles) or 5.6 months (range 0–14.6 months) of atezolizumab. Among the non-AID subgroup, the median treatment exposure was five cycles (range 1–28 cycles) or 2.8 months (range 0–19.0 months). The most common reason for treatment discontinuation in the AID subgroup was disease progression (24 patients; 69%). Five patients discontinued because of AEs (one case each of reactivated sarcoidosis, blood alkaline phosphatase and alanine aminotransferase increased, and psoriasis; one fatal intestinal obstruction on day 182, one unexplained death on day 197) and one was lost

to follow-up after three cycles. The remaining five patients were still on treatment at the data cut-off date.

3.2 Safety

Compared with non-AID patients, a numerically higher proportion of patients in the AID subgroup experienced treatment-related grade 3/4 AEs and AEs of special interest (Table 2). However, there were no relevant increases in treatment-related deaths or AEs leading to atezolizumab discontinuation. The most common AEs in the AID subgroup were fatigue (23%), anaemia (23%) and asthenia (20%) (Supplementary Appendix Fig. A1). The most common grade ≥3 AEs were colitis, gamma-glutamyl transferase (GGT) increased, asthenia and hyponatraemia (Fig. 2). In the AID subgroup, there were three cases of grade 3 colitis, all of which were considered by the investigator to be treatment related; there were no grade 4 or 5 cases of colitis. Of the two patients with pre-existing ulcerative colitis at baseline, one experienced grade 3 colitis and one had no further reported colitis. The two remaining cases of grade 3 colitis during treatment occurred in patients with pre-existing psoriasis. Most other grade ≥3 AEs were not considered treatment related.

Fig. 3 shows AEs of special interest in the AID and non-AID subgroups. Sixteen (46%) of patients in the AID subgroup had an AE of special interest (immune-related); in five patients these were of grade ≥3 intensity (three cases of grade 3 colitis described above, one case of grade 4 increased GGT accompanied by grade 3 increased aspartate aminotransferase and grade 3 rash, and one case of grade 3 increased GGT). The most common grade 1/2 AEs of special interest were rash (grade 1 in four patients) and hypothyroidism (grade 2 in three patients). In the 962 non-AID patients, AEs of special interest were infrequent (6% hypothyroidism, 4% hyperthyroidism, 2% pneumonitis, 1% colitis). In the AID subgroup, pre-existing AID worsened in six patients (17%, including the patient with colitis described above; two flares in two patients). Four of the eight flares subsequently resolved, one was resolving and three were unresolved (Table 3). There was no clear pattern in the timing of flare onset, ranging from day 1 to day 358. All six patients with flares had active AID at baseline, with ongoing treatment for the AID in three of them.

Among 17 patients (49%) in the AID subgroup with grade 3/4 AEs, these AEs had recovered/resolved or were recovering/resolving in seven patients (20%), were unresolved in eight patients (23%) and had worsened to grade 5 in two patients (6%; bowel obstruction, sepsis; both considered unrelated to atezolizumab). The eight patients with unresolved grade 3/4 AEs comprised two cases of grade 3 asthenia and one case each of grade 4 hypercalcaemia, grade 3 pain in extremity, grade 3 pain, grade 3 GGT increase and grade 3 arthralgia/musculoskeletal chest pain (all considered cancer related) and one case of grade 4 GGT increase (considered atezolizumab related). Steroids were administered for AEs in 11 patients with AID; two patients were treated with methotrexate.

3.3 Efficacy

At the data cut-off date, 23 (66%) of the 35 patients with AID had died. The primary cause of death was disease progression in 19 patients (54%), an AE associated with disease progression >30 days after the last atezolizumab dose in two patients (6%), clinical progression in one patient (3%) and unknown cause in one patient (3%). Median OS was 8.2 months (95% CI 6.5–11.7 months) in patients with AID and 8.8 months (95% CI 7.6–9.9 months) in patients without pre-existing AID (Fig. 4). Overall, efficacy was similar in AID and non-AID patients, with overlapping 95% CIs (Table 4).

4. Discussion

To the best of our knowledge, SAUL is the first prospective study of urothelial cancers to include patients with AID. In this subgroup analysis of 35 atezolizumab-treated patients with pre-existing AID and urinary tract carcinoma, incidences of AEs of special interest and treatment-related AEs appeared acceptable, and findings were generally consistent with safety results reported in the overall population of SAUL [20]. AEs were manageable and rarely led to atezolizumab discontinuation. There was no signal of worse clinical outcome in patients with pre-existing AID compared with those without an AID at baseline.

Findings in patients with AID treated with atezolizumab in SAUL are consistent with recent reports in the literature describing various immunotherapy agents in a range of

disease settings, albeit most are in small sample sizes. The 17% incidence of flares (exacerbation of existing AID) in our series of 35 patients is similar to or lower than incidences reported in recently published retrospective analyses [15]. In a prospective study of 45 patients with AID (most commonly vitiligo and psoriasis) and non-urothelial tumour types (predominantly melanoma) treated with PD-1 inhibitors in the REISAMIC registry, immune-related AEs developed in 44% of patients and flares of AIDs were reported in 24% [16]. Among patients developing immune-related AEs, one-quarter required treatment discontinuation. In a systematic literature review of 123 patients with pre-existing AID who were treated with various checkpoint inhibitors, most flares and immune-related AEs were manageable with corticosteroids and improved without discontinuing immunotherapy in more than half of the patients [21]. In a retrospective cohort of 112 patients with pre-existing AID (most commonly psoriasis or rheumatoid arthritis) treated with immune checkpoint inhibitors in French centres, flares of pre-existing AID were reported in approximately half of the patients, yet only 21% required discontinuation of immunotherapy [14]. In a smaller study (*n* = 22) specifically in patients with rheumatoid arthritis treated with immune checkpoint inhibitors, a similar proportion of patients with flares was observed (55%), most of which were managed with oral corticosteroids [22]. Finally, in a retrospective analysis of 56 patients with non-small-cell lung cancer and pre-existing AID (predominantly rheumatoid arthritis or psoriasis) treated with PD-1 or PD-L1 inhibitors, 23% of patients experienced AID flares, but immune-related AEs were generally manageable and only 14% of patients required permanent discontinuation of immunotherapy because of immune-related AEs [23]. Interestingly, Leonardi et al. noted that flares were more common in patients with rheumatologic than non-rheumatologic AIDs, and more common in patients with active/symptomatic AID when immunotherapy was initiated than in those without symptomatic AID at the start of immunotherapy [23]. This is consistent with the recognised increase in cytokine levels in more advanced stages of both AID and cancer [7]. In our study, none of the four patients with rheumatologic AID experienced flares, but with small sample sizes no definitive conclusions can be drawn.

In the SAUL study in urothelial carcinoma, efficacy outcomes suggest that atezolizumab is as effective in patients with AID as in those without. A similar conclusion was reached by Danlos et al. based on their case series of patients receiving anti-PD-1 therapy for a range of cancers [16]. Efficacy findings are also consistent with a recently reported retrospective analysis of real-world data in AID patients with various cancers (predominantly lung cancer and melanoma) treated with PD-L1, PD-1 or cytotoxic T-lymphocyte antigen-4 (CTLA-4) inhibitors alone or in combination [24].

The authors of the French retrospective study described above noted that PFS was shorter in patients receiving immunosuppressive therapy at the start of immunotherapy compared with those who were not receiving immunosuppressive therapy, and shorter in those who experienced a flare of their pre-existing AID compared with those who did not [14]. The sample size in our study is too small to determine whether immunosuppressive therapy or AID flares were associated with worse efficacy outcome; however, PFS was not diminished in patients with pre-existing AID compared with non-AID patients (median 4.4 vs 2.2 months, respectively).

Although SAUL included only 35 patients with AID, to date this is the largest reported series of patients with urothelial carcinoma and AID treated with checkpoint blockade. An important strength of these findings is that these were prespecified analyses of data from a prospective study specifically designed to assess outcomes in special populations of patients and had a co-registered prospective non-AID group. Outcomes can therefore be compared between the AID and non-AID subgroups, all of whom were treated with an identical regimen, with homogeneous efficacy and safety assessments, data collection and follow-up. The single-arm design of the parent study, however, prevents comparison of atezolizumab with other treatments.

The results from this study should not be extrapolated to all AIDs, as a large proportion of patients had psoriasis, thyroid disease or rheumatoid arthritis, similar to other reports in the literature. None of the patients had myasthenia gravis and patients with life-threatening diseases other than cancer were not eligible for SAUL, an approach in line with

recently published National Comprehensive Cancer Network (NCCN) guidelines recommending against immunotherapy in such patients [15,25]. In SAUL, both of the patients with ulcerative colitis had active AID requiring treatment at baseline, and one of them experienced a flare. In a recent study of patients with ulcerative colitis or Crohn's disease receiving immunotherapy, there was an increased risk of gastrointestinal AEs, including colonic perforation [26].

Recently, an international panel of oncologists and immunologists proposed a personalised risk-based strategy for the use of immune checkpoint inhibitors in patients with AID [19]. Among the recommendations, the authors describe a strategy to replace non-selective immunosuppressants with specific selective immunosuppressant drugs to lessen the risk of compromising the efficacy of immune checkpoint inhibitors. Subsequently, the immune checkpoint inhibitor could be combined with the selective immunosuppressant to prevent exacerbation of the AID. Although such approaches are not recommended in non-specialist settings, the authors advocate international collaboration to collect prospective data on such strategies.

In conclusion, findings from this prespecified analysis provide reassurance that AID does not preclude atezolizumab treatment for patients with urothelial cancer. Atezolizumab treatment for patients with AID requires caution, but AID is not intrinsically a barrier to atezolizumab therapy. Results from our prespecified analysis of 35 patients with AID treated with atezolizumab in the SAUL study are consistent with recent recommendations made by the NCCN [15]. For patients with pre-existing AID in whom immunotherapy is being considered, multidisciplinary review, including involvement of the patient's AID specialist, is recommended.

Role of the funding source

The sponsor played a role in the design and conduct of the study; data collection, management, analysis, and interpretation; and preparation, review, and approval of the manuscript.

Data statement

Qualified researchers may request access to individual patient-level data through the clinical study data request platform (https://vivli.org/). Further details on Roche's criteria for eligible studies are available here (https://vivli.org/members/ourmembers/). For further details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here (https://www.roche.com/research_and_development/who_we_are_how_we_work/clinical_trials/our_commitment_to_data_sharing.htm).

Contributor statement

Y. Loriot, C.N. Sternberg, D. Castellano, S. de Ducla and E. Choy were involved in the study concept and design. Y. Loriot, C.N. Sternberg, D. Castellano, S.F. Oosting, H. Dumez, R. Huddart, K. Vianna, T. Alonso Gordoa, I. Skoneczna, A.P. Fay, F. Nolè, F. Massari, B. Brasiuniene and P. Maroto were involved in data acquisition. S. Fear was responsible for data quality control and statistical analysis. All authors were responsible for data interpretation and manuscript preparation, editing and review.

Conflict of interest

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Figure legends

Fig. 1. Autoimmune conditions at baseline in the AID subgroup (*n* = 35). Includes three patients with two AIDs (all had psoriasis and thyroid conditions).

AID, autoimmune disease.

Fig. 2. Grade ≥3 AEs in the AID subgroup.

AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

[a]Patient with intestinal obstruction also had colitis.

Fig. 3. AEs of special interest (worst grade) in >1 patient in either group according to AID.

[a] 2.8% = 1 patient, 5.7% = 2 patients, 8.6% = 3 patients.

AID, autoimmune disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase.

Fig. 4. Overall survival according to presence of AID at baseline.

AID, autoimmune disease; CI, confidence interval.

Supplementary Appendix Fig. A1

Most common (>10% of patients) adverse events of any grade in the autoimmune disease subgroup (*n* = 35).

Table 1

Baseline characteristics according to AID.

Characteristic	Non-AID subgroup (*n* = 962)	AID subgroup (*n* = 35)
Median age, years (range)	68 (34–93)	69 (41–82)
Age, years, *n* (%)		
≥65	595 (62)	25 (71)
≥80	77 (8)	1 (3)
Male, *n* (%)	746 (78)	26 (74)
PD-L1 status, *n* (%)		
IC 0	234 (24)	9 (26)
IC 1	405 (42)	16 (46)
IC 2/3	256 (27)	8 (23)
Missing	67 (7)	2 (6)
ECOG performance status, *n* (%)		
0	414 (43)	13 (37)
1	450 (47)	19 (54)
2	98 (10)	3 (9)
Tumour location, *n* (%)		
Bladder	716 (74)	28 (80)
Urethra	10 (1)	0
Ureter	95 (10)	2 (6)
Renal pelvis	118 (12)	4 (11)
Other	23 (2)	1 (3)
Steroid at baseline, *n* (%)	38 (4)	2 (6)
Non-urothelial/mixed histology, *n* (%)	44 (5)	3 (9)

CNS metastases, *n* (%)	13 (1)	1 (3)
Renal impairment, *n* (%)	45 (5)	1 (3)
Prior lines of treatment for metastatic disease, *n* (%)		
0	370 (38)	12 (34)
1	522 (54)	21 (60)
2	51 (5)	1 (3)
3	19 (2)	1 (3)

AID, autoimmune disease; CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; IC, immune cell; IC 0, PD-L1 expression on <1% of tumour-infiltrating ICs; IC 1, PD-L1 expression on ≥1% but <5% of tumour-infiltrating ICs; IC 2/3, PD-L1 expression on ≥5% of tumour-infiltrating ICs; PD-L1, programmed cell death ligand-1.

Table 2

Overview of safety according to AID.

AE, *n* (%)	Non-AID subgroup (*n* = 962)	AID subgroup (*n* = 35)
Any-grade AE	848 (88)	32 (91)
Grade 3/4	414 (43)	17 (49)
Grade 5	34 (4)	3 (9)[a]
Treatment-related AE	506 (53)	24 (69)
Grade 3/4	112 (12)	9 (26)
Grade 5	7 (1)	0
Serious AE	316 (33)	11 (31)
AE of special interest	289 (30)	16 (46)
Grade ≥3	62 (6)	5 (14)

[a] One case each of sepsis, intestinal obstruction and unexplained death.

AE, adverse event; AID, autoimmune disease.

Table 3

Details of autoimmune flares.

AID at baseline	Status of AID at study entry	Other relevant conditions at baseline	AE	Onset day	AE related to AID	AE related to atezo-lizumab	Atezo-lizumab discon-tinued	Steroid	Other immuno-suppressant	Outcome	Best overall response	DoR, months	PFS, months	OS, months
Psoriasis	Ongoing without treatment	Diabetes mellitus, rash, hypomagnesaemia, haemochromatosis, Gilbert's syndrome	Grade 1 rash (became grade 2)	21 (grade 2 day 155)	Yes	Yes	No	No	Yes	Recovered/ resolved	SD	–	12.2	13.6
			Grade 1 neurodermatitis, dermatitis psoriasiform, actinic keratosis	343		Yes			No	Unresolved				
Psoriasis	Ongoing with clobetasol and fluocinolone acetonide treatment	Rash	Grade 2 psoriasis	71	Yes	Yes	Yes	No	Yes	Unresolved	NA	NA	11.1[a]	13.2[a]
Ulcerative colitis	Ongoing with dexamethas-one	Hypercalcaemia, hypohosphataemia	Grade 3 hypercalcaemia (became SAE,	1 (SAE day	No	No	No	No	No	Unresolved	NA	–	2.4	2.4

	treatment, concomitant steroid		then grade 4); grade 3 hyper-kalaemia (SAE)	19, grade 4 day 31); 19											
Ulcerative colitis	Ongoing with prednisone treatment	Pericarditis, hyperhidrosis	Grade 1 increased transaminases, grade 3 colitis (SAE)	62 76	Yes	Yes Yes	No	Yes	No	Recovering Recovered/ resolved	PD	–	2.7	11.7	
Sarcoidosis	Ongoing without treatment	Type 2 diabetes mellitus	Grade 4 sarcoidosis (SAE)	358	Yes	Yes	Yes	Yes	No	Recovered/ resolved	PR	10.6	12.6	15.4[a]	
Primary biliary cirrhosis	Ongoing without treatment	Primary biliary cholangitis, hyponatraemia	Grade 3 hyponatraemia (SAE)	15	No	No	No	No	No	Recovered/ resolved	PD	–	0.9	2.7	

[a] Censored at data cut-off.

AE, adverse event; AID, autoimmune disease; DoR, duration of response; NA, not available; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; SAE, serious adverse event; SD, stable disease.

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Commented [JEK2]: Reviewer 2: only worsened ionic abnormalities (hypercalcemia and hyponatremia). These ionic abnormalities are usually not related to AID. Why did the authors consider the worsening of ionic abnormalities as a flare of the AID

Table 4

Overview of efficacy according to AID.

Parameter	Non-AID subgroup (*n* = 969)	AID subgroup (*n* = 35)
Deaths, *n* (%)	532 (55)	23 (66)
Median OS, months [95% CI]	8.8 [7.6–9.9]	8.2 [6.5–11.7]
6-month OS rate, % [95% CI]	59 [56–63]	74 [56–86]
1-year OS rate, % [95% CI]	42 [38–45]	31 [16–48]
PFS events, *n* (%)	769 (79)	28 (80)
Median PFS, months [95% CI]	2.2 [2.1–2.3]	4.4 [2.2–6.3]
ORR, n (%)[a] [95% CI]	131 (14) [11–16]	4 (11) [3–27]
Disease control rate, *n* (%)[b] [95% CI]	380 (39) [36–42]	18 (51) [34–69]

[a] Confirmed complete or partial response per Response Evaluation Criteria in Solid Tumours (version 1.1).

[b] Sum of confirmed complete or partial responses, plus stable disease for ≥4 weeks.

AID, autoimmune disease; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.