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PRECISION ONCOLOGY CONNECT

MEETING HIGHLIGHTS FROM ASCO AND WCIGC 2023

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CLINICAL TAKEAWAYS

- **DESTINY-PanTumour02:** Study shows T-DXd to be a potential new treatment option for patients with HER2-expressing solid tumours, with higher efficacy in IHC 3+ and efficacy also in anti-HER2 pre-treated patients
- **KontRASt-01:** JDQ443 exhibits potent antitumour activity in NSCLC with good disease control and partial responses as well as a good tolerability profile
- **ADVL1823:** First data in first-line treatment with larotrectinib in the NTRK+ infantile fibrosarcoma population, with data suggesting that local control (surgery) remains important to achieve long-term results
- **Molecular Profiling in Biliary Cancers (BTC):** the study highlights the importance of conducting NGS upfront for BTC. Treatment with a matched targeted therapeutic provides benefit in terms of DCR, PFS and OS

BTC, biliary tract cancer; CR, complete response; DCR, disease control rate; HER2, human epidermal growth factor receptor 2; MTA, molecularly targetable agent; NGS, next generation sequencing; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; PR, partial response; T-DXd, trastuzumab deruxtecan

EDUCATIONAL OBJECTIVES

- Help physicians translate the latest Precision Oncology data from ASCO 2023 and WCIGC 2023 into clinical practice

EFFICACY AND SAFETY OF TRASTUZUMAB DERUXTECAN IN PATIENTS WITH HER2-EXPRESSING SOLID TUMOURS: DESTINY-PANTUMOR02 INTERIM RESULTS

Meric-Bernstam F, et al. ASCO 2023. Abstract #LBA3000

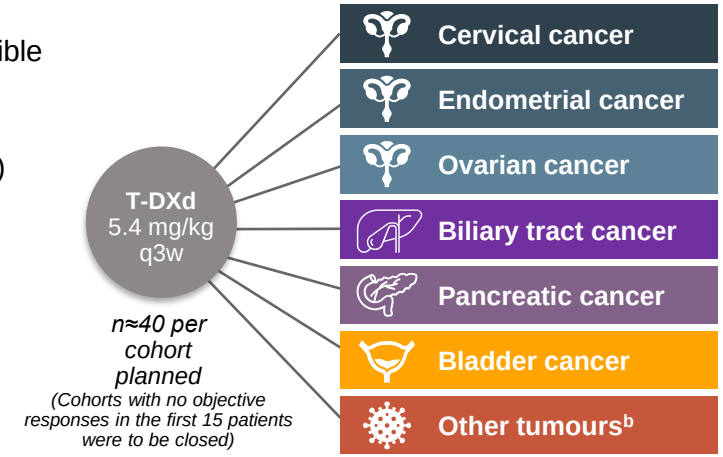
HER2, human epidermal growth factor receptor 2

DESTINY-PANTUMOUR02: BACKGROUND AND STUDY DESIGN

- T-DXd is an antibody drug conjugate targeting HER2 and is approved in HER2-expressing breast and gastric cancers[1]
- HER2 expression is prevalent in other solid tumours. The efficacy of current treatments (Tx) in these populations, including studies with HER2-directed Tx, is modest, revealing a significant unmet medical need[1]
- Clinically meaningful activity of T-DXd was seen in HER2-expressing tumours in a phase 1 study (NCT02564900)[1]
- This is the first tumour-agnostic global study of T-DXd in a broad range of HER2-expressing solid tumors[1]

An open-label, multicentre study (NCT04482309)[1]

- Advanced solid tumours not eligible for curative therapy
- 2L+ patient population
- HER2 expression (IHC 3+ or 2+)
  - Local test or central test by Hercep Test if local test not feasible (ASCO/CAP gastric cancer guidelines[2])[a]
- Prior HER2-targeting therapy allowed
- ECOG/WHO PS 0-1



Primary endpoint

- Confirmed ORR (investigator)[c]

Secondary endpoints

- DoR[c]
- DCR[c]
- PFS[c]
- OS
- Safety

Data cut-off for analysis:

- Nov 16, 2022

[a] Patients were eligible for either test. All patients were centrally confirmed. [b] Patients with tumours that express HER2, excluding tumours in the tumour-specific cohorts, and breast cancer, NSCLC gastric cancer and CRC; [c]Investigator-assessed per Response Evaluation Criteria in Solid Tumours version 1.1

2L, second line; ASCO, American Society of Oncology; CAP, College of American Pathologists; DCR, disease control rate; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PS, performance status; q3w, every 3 weeks; T-DXd, trastuzumab deruxtecan; WHO, World Health Organisation

1. Meric-Bernstam F, et al. J Clin Oncol. 2023;41 (suppl 17); abstr LBA3000) (Oral presentation); 2. Hofmann M, et al. Histopathology. 2008;52(7):797-805

DESTINY-PANTUMOUR02: EFFICACY RESULTS

		Cervical (n=40)	Endometrial (n=40)	Ovarian (n=40)	BTC (n=41)	Pancreatic (n=25)	Bladder (n=41)	Other (n=40)	All patients (N=267)
Investigator assessment									
ORR, n (%)		**20 (50.0)**	**23 (57.5)**	**18 (45.0)**	**9 (22.0)**	**1 (4.0)**	**16 (39.0)**	**12 (30.0)**	**99 (37.1)**
Best overall response, n (%)	Complete response	2 (5.0)	7 (17.5)	4 (10.0)	1 (2.4)	0	1 (2.4)	0	15 (5.6)
	Partial response	18 (45.0)	16 (40.0)	14 (35.0)	8 (19.5)	1 (4.0)	15 (36.6)	12 (30.0)	84 (31.5)
	Stable disease	12 (30.0)	13 (32.5)	14 (35.0)	25 (61.0)	17 (68.0)	18 (43.9)	24 (60.0)	123 (46.1)
	PD	7 (17.5)	4 (10.0)	7 (17.5)	7 (17.1)	7 (28.0)	7 (17.1)	3 (7.5)	42 (15.7)
	Not evaluable	1 (2.5)	0	1 (2.5)	0	0	0	1 (2.5)	3 (1.1)
DCR[a] at 12 weeks, n (%)		27 (67.5)	32 (80.0)	28 (70.0)	27 (65.9)	9 (36.0)	29 (70.7)	30 (75.0)	182 (68.2)
Median DoR, months (95% CI)		9.8 (4.2-NE)	NR (9.9-NE)	11.3 (4.1-NE)	8.6 (2.1-NE)	NR	8.7 (4.3-11.8)	NR (4.1-NE)	11.8 (9.8-NE)
Independent central review: ORR, n (%)		16 (40.0)	21 (52.5)	17 (42.5)	11 (26.8)	3 (12.0)	17 (41.5)	13 (32.5)	98 (36.7)

Analysis of response and DCR was performed in patients who received ≥1 dose of T-DXd (N=267). Analysis of DoR was performed in patients with objective response who received ≥1 dose of T-DXd (n=99)

[a] Confirmed complete response, confirmed partial response or stable disease

	All patients (n=99)	IHC 3+ (n=46)	IHC 2+ (n=34)
Median DoR, months (95% CI)	11.8 (9.8-NE)	22.1 (9.3-NE)	9.8 (4.2-12.6)

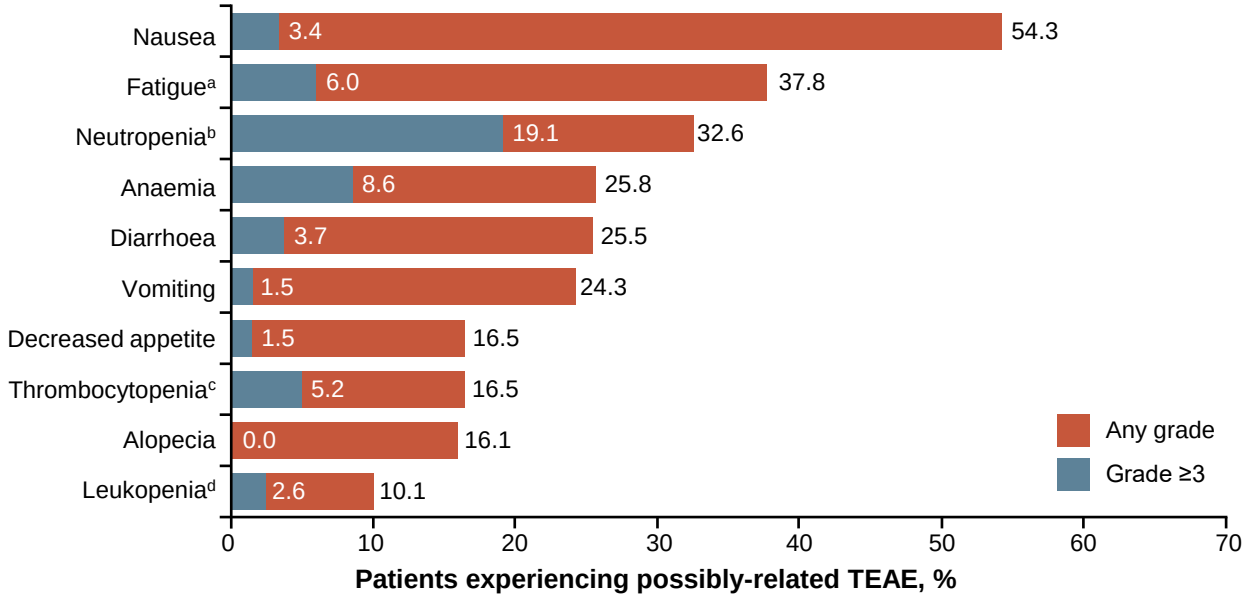
BTC, biliary tract cancer; CI, confidence interval; DCR, disease control rate; DoR, duration of response; NE, not evaluable; NR, not reached; ORR, objective response rate; PD, progressive disease; T-DXd, trastuzumab deruxtecan

Meric-Bernstam F, et al. J Clin Oncol. 2023;41 (suppl 17); abstr LBA3000) (Oral presentation)

DESTINY-PANTUMOUR02: SAFETY RESULTS

- Grade ≥3 drug-related TEAEs occurred in 38.6% of pts; 8.2% discontinued Tx due to drug-related TEAEs

DRUG-RELATED TEAEs IN ≥10% OF PATIENTS



Analyses were performed in patients who received ≥1 dose of T-DXd (n=267). [a] Includes preferred terms of fatigue, asthenia and malaise. [b] Includes preferred terms of neutrophil count decreased and neutropenia. [c] Includes preferred terms of platelet count decreased and thrombocytopenia. [d]Includes preferred terms of WBC decreased and leukopenia

ADVERSE EVENTS OF SPECIAL INTEREST

ILD/pneumonitis adjudicated as T-DXd–related						
n (%)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Any grade**
All patients	6 (2.2)	12 (4.5)	1 (0.4)	0	1 (0.4)	20 (7.5)
Left ventricular dysfunction[a]						
n (%)	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**	**Any grade**
Ejection fraction decreased						
All patients	1 (0.4)	4 (1.5)	1 (0.4)	0	0	7 (2.6)[b]
Cardiac failure						
All patients	0	0	1 (0.4)	0	0	1 (0.4)

Analyses were performed in patients who received ≥1 dose of T-DXd (n=267). [a] Left ventricular dysfunction was reported in a total of 12 (4.5%) patients, of which 8 (3.0%) were considered possibly T-DXd related. [b] One patient had unknown grade of ejection fraction decrease

ILD, interstitial lung disease; T-DXd, trastuzumab deruxtecan; TEAEs, treatment-emergent adverse events; Tx, treatment; WBC, white blood cells

Meric-Bernstam F, et al. J Clin Oncol. 2023;41 (suppl 17); abstr LBA3000) (Oral presentation)

DESTINY-PANTUMOUR02: SUMMARY

- Interim results of the phase 2 trial DESTINY-PanTumor-02 show that T-DXd has broad activity across HER-2+ tumour types and a toxicity profile consistent with previous studies
- T-DXd had the lowest activity in pancreatic cancer, and this cohort was stopped early
- Responses were especially high among patients who had cervical, endometrial, and ovarian cancers

Clinical Perspective

- **The study shows T-DXd to be a potential new treatment option for patients with HER2-expressing solid tumours**
- **High response rate achieved in almost all histologies, with better activity in IHC 3+**
- **It is possible to achieve response and clinical benefit with T-DXd treatment also in patients previously treated with anti-HER2 targeted treatment**

HER2, human epidermal growth factor receptor 2; T-DXd, trastuzumab deruxtecan

Meric-Bernstam F, et al. J Clin Oncol. 2023;41 (suppl 17); abstr LBA3000) (Oral presentation); https://dailynews.ascopubs.org/do/destiny-pantumor-02-trastuzumab-deruxtecan-has-activity-against-range-her2-expressing#:~:text=in%20the%20study.-,T%2DDXd%20had%20the%20lowest%20activity%20in%20pancreatic%20cancer%2C%20and,Meric%2DBernstam%20said

KontRASt-01 UPDATE: SAFETY AND EFFICACY OF JDQ443 IN *KRAS G12C*-MUTATED SOLID TUMOURS INCLUDING NSCLC

Cassier PA, et al. ASCO 2023. Abstract #9007

KRAS, Kirsten rat sarcoma viral oncogene homolog; NSCLC, non-small cell lung cancer

KontRASt-01: BACKGROUND STUDY DESIGN

- **JDQ443** is a selective, covalent, orally bioavailable **KRAS^{G12C} inhibitor** that irreversibly traps KRAS^{G12C} in the inactive, GDP-bound state
- **KontRASt-01** (NCT04699188) is a **Phase 1b/2, open-label, multicentre, dose-escalation, and dose-expansion trial** of JDQ443 as a monotherapy or in combination with TNO155 (SHP2 inhibitor) and/or tislelizumab (anti–PD-1 monoclonal antibody)

Eligibility

- Patients with advanced, *KRAS G12C*-mutated solid tumours who have received SoC therapy or who are intolerant of or ineligible for approved therapies;
- ECOG PS 0-1;
- no prior treatment with a KRAS^{G12C} inhibitor

Dose escalation: Phase 1b	Food effect (FE)[a]	Dose expansion: Phase 2
KRAS G12C-mutated solid tumours (n=39)	KRAS G12C-mutated solid tumours (n=15)	• KRAS G12C-mutated NSCLC (n=22) • KRAS G12C-mutated CRC (n=20)
200 mg QD / 400 mg QD 200 mg BID / 300 mg BID	Monotherapy RD for expansion: 200 mg BID	

- **Key objectives for dose escalation phase:** safety/tolerability; MTD/RD, anti-tumour activity, PD
- **Key objectives for dose expansion phase:** JDQ443 anti-tumour activity (monotherapy), safety/tolerability, PK

Data presented are from a cut-off date of Feb 1, 2023.

[a] Patients in the FE cohort received treatment on an empty stomach at least 1 hour before and 2 hours after a meal from Day 1 to Day 7. Following a washout period with no treatment on Day 8, patients commenced standard treatment cycles at the same dose and schedule, receiving JDQ443 with food. For dose escalation and dose expansion, JDQ443 was dosed with food at all time points.

BID, twice daily; CRC, colorectal cancer; ECOG, Eastern Cooperative Oncology Group; GDP, guanosine diphosphate; KRAS, Kirsten rat sarcoma viral oncogene homolog; MTD, maximum tolerated dose; NSCLC, non-small cell lung cancer; PD, pharmacodynamics; PD-1, programmed cell death protein 1; PK, pharmacokinetics; PS, performance status; QD, once daily; RD, recommended dose; SHP2, Src homology-2 domain-containing protein tyrosine phosphatase-2; SoC, standard of care

Cassier PA, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 9007) (Oral presentation)

KontRASt-01: BASELINE CHARACTERISTICS

DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	JDQ443 200 mg QD escalation (n=10)	JDQ443 400 mg QD escalation (n=11)	JDQ443 300 mg BID escalation (n=7)	JDQ443 200 mg BID escalation + FE + expansion (n=68)	All dose levels, pooled (N=96)
Age (years)					
Median	57.0	63.0	59.0	62.5	61.5
Range (min-max)	(30.0-73.0)	(50.0-76.0)	(27.0-72.0)	(26.0-83.0)	(26.0-83.0)
Sex, n (%)					
Female	5 (50.0)	7 (63.6)	5 (71.4)	33 (48.5)	50 (52.1)
Number of prior lines of antineoplastic therapy					
Median	3	3	3	2	2
Range (min-max)	(1-5)	(1-7)	(2-6)	(1-7)	(1-7)
History of prior ICI therapy, n (%)					
Yes	5 (50.0)	7 (63.5)	–	33 (48.5)	45 (46.9)
ECOG PS, n (%)					
0	2 (20.0)	5 (45.5)	5 (71.4)	26 (38.2)	38 (39.6)
1	8 (80.0)	6 (54.5)	2 (28.6)	42 (61.8)	58 (60.4)
History of CNS metastasis, n (%)					
Yes	1 (10.0)	2 (18.2)	–	8 (11.8)	11 (11.5)
No	9 (90.0)	8 (72.7)	7 (100.0)	59 (86.8)	83 (86.5)
Unknown	–	1 (9.1)	–	1 (1.5)	2 (2.1)
Indication, n (%)					
NSCLC	6 (60.0)	7 (63.6)	–	36 (52.9)	49 (51.0)
CRC	4 (40.0)	3 (27.3)	6 (85.7)	30 (44.1)	43 (44.8)
Other[a]	–	1 (9.1)	1 (14.3)	2 (3.0)	4 (4.2)

Data presented with a cut-off date of Feb 1, 2023. Among patients with NSCLC, 89.8% (44/49) had a history of prior ICI therapy

[a] Other indications included one each of: Appendix cancer, bile duct cancer, ovarian cancer and pancreatic cancer

BID, twice daily; BOR, best overall response; CNS, central nervous system; CRC, colorectal cancer; DCR, disease control rate; ECOG, Eastern Cooperative Oncology Group; FE, food effect; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; PS, performance status; QD, once daily; SD, stable disease

Cassier PA, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 9007) (Oral presentation)

KontRASt-01: SAFETY RESULTS

TREATMENT-RELATED ADVERSE EVENTS (≥10% OF ALL PATIENTS)

- TRAEs were low-frequency, low-grade events
- There were no Grade 4 or 5 TRAEs
- No nausea/vomiting/diarrhoea higher than Grade 2

	JDQ443 200 mg QD escalation (n=10)		JDQ443 400 mg QD escalation (n=11)		JDQ443 300 mg BID escalation (n=11)		JDQ443 200 mg BID escalation + FE + expansion (n=68)		All dose levels, pooled (N=96)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Patients with at least one event, n (%)	**8 (80.0)**	**2 (20.0)**	**8 (72.7)**	**1 (9.1)**	**6 (85.7)**	**5 (71.4)**	**51 (75.0)**	**4 (5.9)**	**73 (76.0)**	**12 (12.5)**
Fatigue	5 (50.0)	2 (20.0)	3 (27.3)	–	4 (57.1)	1 (14.3)	11 (16.2)	–	23 (24.0)	3 (3.1)
Nausea	3 (30.0)	–	1 (9.1)	–	–	–	12 (17.6)	–	16 (16.7)	–
Diarrhoea	2 (20.0)	–	2 (18.2)	–	1 (14.3)	–	9 (13.2)	–	14 (14.6)	–
Peripheral oedema	2 (20.0)	–	2 (18.2)	–	1 (14.3)	–	8 (11.8)	–	13 (13.5)	–
Neutropenia	–	–	1 (9.1)	–	2 (28.6)	1 (14.3)	8 (11.8)	2 (2.9)	11 (11.5)	3 (3.1)
Vomiting	2 (20.0)	–	–	–	–	–	8 (11.8)	–	10 (10.4)	–
Anaemia	2 (20.0)	–	2 (18.2)	–	–	–	6 (8.8)	–	10 (10.4)	–

Data presented with a cut-off date of Feb 1, 2023. All AEs were graded per CTCAE version 5.0. Two patients experienced treatment-related SAEs: Grade 3 photosensitivity reaction and Grade 2 rash erythematous in one patient; Grade 3 bullous dermatitis in one patient (all occurred at 300 mg BID). Treatment was discontinued by three patients for TRAEs. Two patients due to elevated ALT and one due to nauseas, diarrhoea and vomiting. Seven patients had dose reductions across the following groups: 200mg QD (n=2), 200 mg BID (n=2) and 300mg BID (n=3). Two patients from the 200 mg bid group had dose reductions: one patient due to Grade 3 ALT elevation and Grade 3 AST elevation, and one patient due to Grade 2 peripheral neuropathy

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BID, twice daily; CTCAE, common terminology criteria for adverse events; FE, food effect; QD, once daily; SAE, serious adverse event; TRAE, treatment-related adverse event

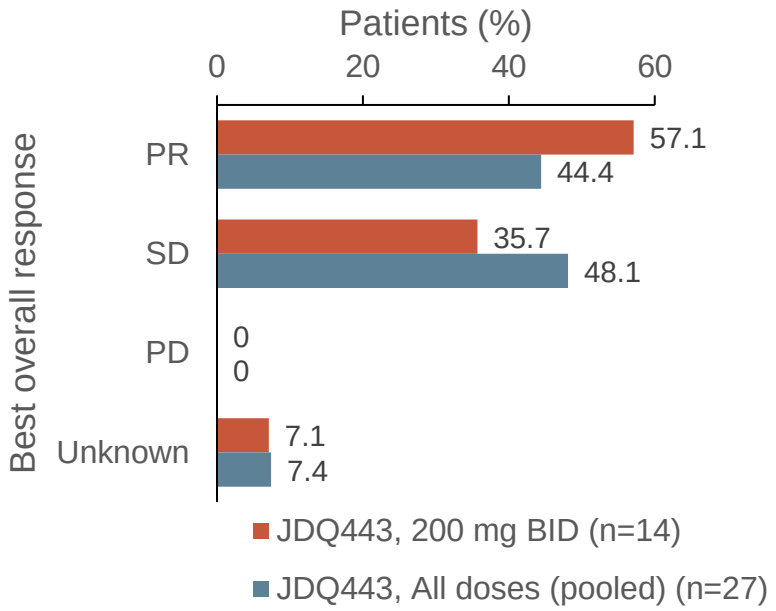
Cassier PA, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 9007) (Oral presentation)

KontRASt-01: EFFICACY RESULTS

NSCLC: BEST OVERALL RESPONSE

	JDQ443 200 mg BID (n=14)	JDQ443 All dose levels, pooled (n=27)
Confirmed (%)		
ORR	**57.1%**	**44.4%**
DCR	92.9%	92.6%

Efficacy dataset: patients with **NSCLC** (N=27) from dose escalation and FE cohorts



Data presented with a cut-off date of Feb 1, 2023. Among patients with NSCLC, 89.8% (44/49) had a history of prior ICI therapy

BID, twice daily; CNS, central nervous system; CRC, colorectal cancer; DCR, disease control rate; ECOG, Eastern Cooperative Oncology Group; FE, food effect; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; ORR, objective response rate; PD, progressive disease; PR, partial response; PS, performance status; SD, stable disease

Cassier PA, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 9007) (Oral presentation)

KontRASt-01: SUMMARY

- JDQ443 exhibits antitumour activity in NSCLC
- JDQ443 demonstrates an acceptable safety and tolerability profile at 200 mg BID, with clinical activity in patients with NSCLC
- Enrolment is ongoing to the JDQ443 monotherapy dose expansion and the JDQ443 + TNO155 and JDQ443 + tislelizumab combination arms

Clinical Perspective

- **JDQ443 exhibits anti-tumour activity in NSCLC with good disease control and partial responses**
- **Interesting to see further development of this compound due to its potent activity and good tolerability profile, particularly with respect to combination studies with anti-PD1 and other inhibitors of the KRAS axis**

BID, twice daily; KRAS, Kirsten rat sarcoma virus; NSCLC, non-small cell lung cancer; PD1, programmed death-1

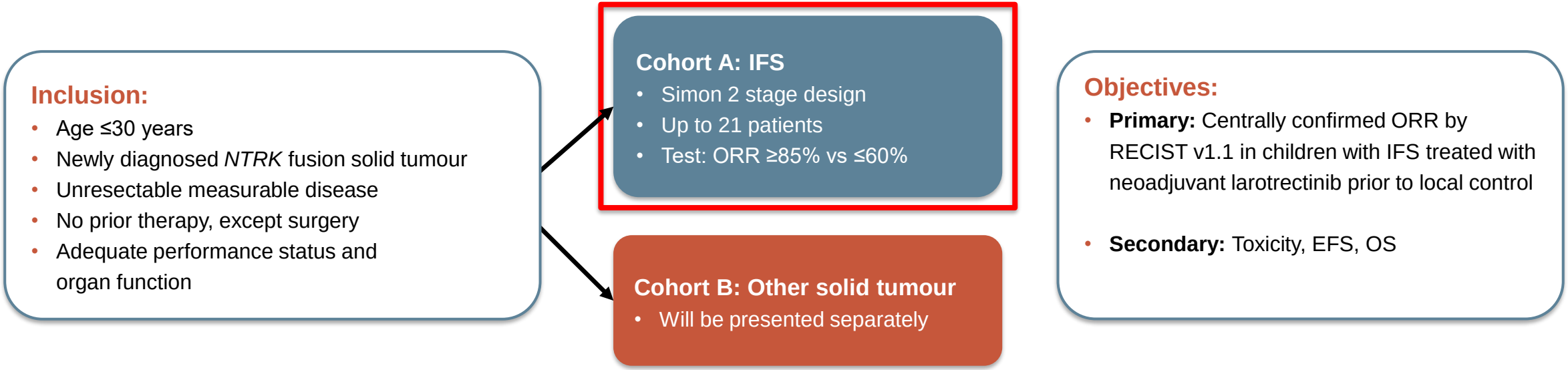
Cassier PA, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 9007) (Oral presentation)

PHASE 2 STUDY OF LAROTRECTINIB IN CHILDREN WITH NEWLY DIAGNOSED INFANTILE FIBROSARCOMA: CHILDREN'S ONCOLOGY GROUP ADVL1823 COHORT A

Laetsch TW, et al. ASCO 2023. Abstract #10008

ADVL1823: BACKGROUND AND STUDY DESIGN

- *NTRK1/2/3* gene fusions (TRK fusions) occur in a range of paediatric cancers and are the canonical molecular alterations in IFS
- Larotrectinib is a highly selective TRK inhibitor that is FDA-approved for TRK fusion solid tumours in patients with no satisfactory alternative treatments or whose cancer has progressed following initial treatment
- ADVL1823 (NCT03834961) evaluated larotrectinib in children with newly diagnosed TRK fusion positive solid tumours in two histology-based cohorts
- Cohort A enrolled patients with IFS and is the focus of this analysis



Data-cut Dec 31, 2022. Central review of imaging submitted before this date is included, despite review occurring after the data cut. One DLT occurring before the data cut but reported afterwards is included.

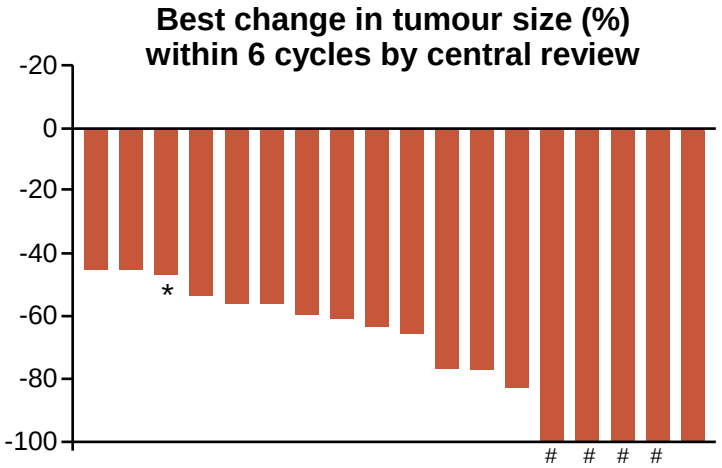
EFS, event-free survival; FDA, Food and Drug Administration; IFS, infantile fibrosarcoma; NTRK, neurotrophic tyrosine receptor kinase; ORR, objective response rate; OS, overall survival; RECIST, Response Evaluation Criteria in Solid Tumours; TRK, tropomyosin receptor kinase

Laetsch TW, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 10008) (Oral presentation)

ADVL1823: EFFICACY RESULTS

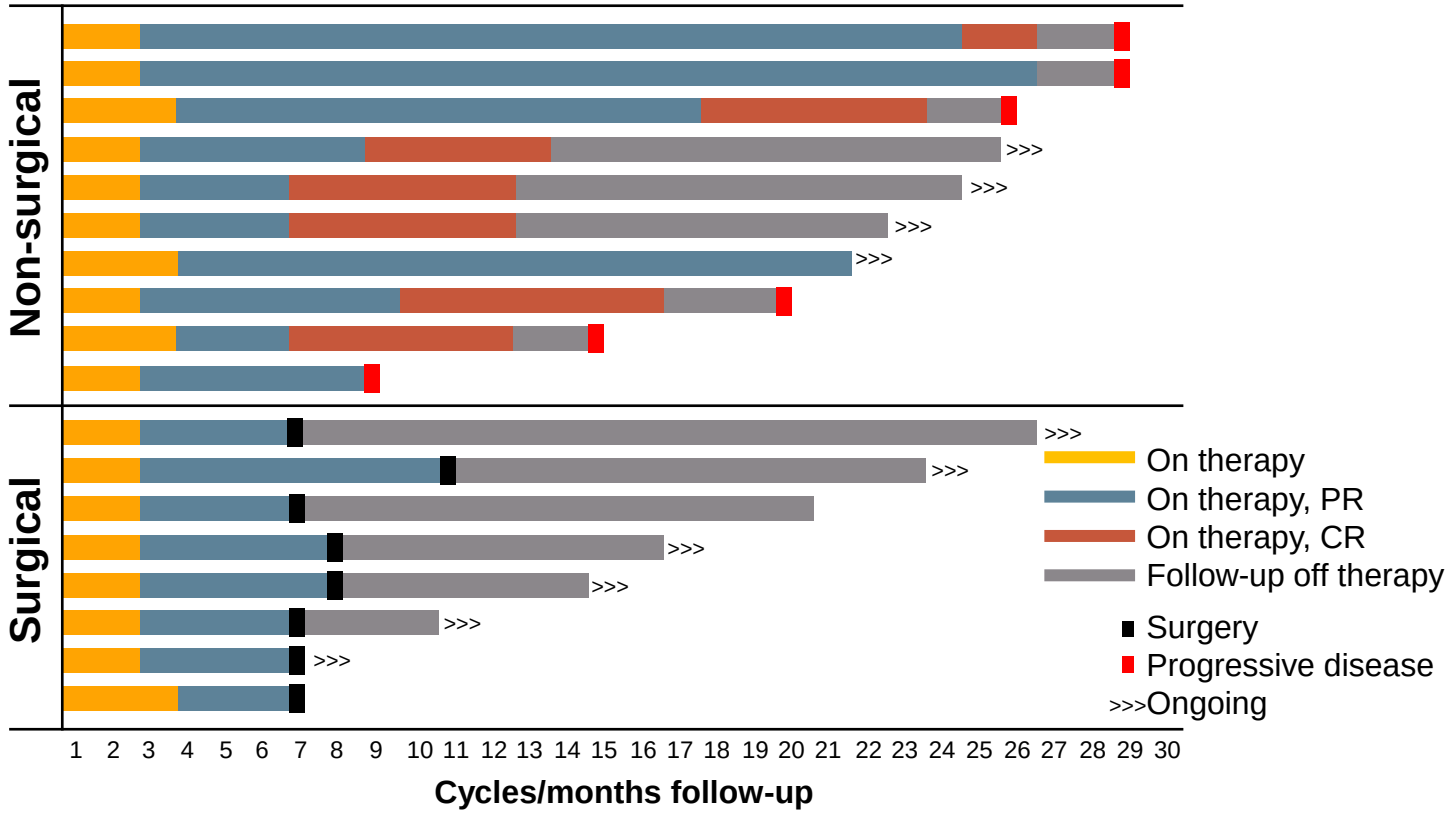
- 94% overall response rate within the first six cycles of treatment

Confirmed response by central review, n (%)	N=18
Overall response rate	17 (94)
Complete response	1 (6)
Partial response	16 (89)
Non-responder*	1 (6)
Progressive disease	0



* Patient with 47% tumour reduction after cycle 2 by central review (79% by investigator), but no confirmatory scan obtained within six cycles; # Partial responder (complete response was not confirmed within six cycles). Each bar represents a single patient

- 70% of non-surgical patients reported CR
- All surgical patients remain progression-free



Each bar represents a single patient

CR, complete response; PR, partial response

Laetsch TW, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 10008) (Oral presentation)

ADVL1823: SAFETY RESULTS

- 7 of 18 (39%) patients had treatment-related CTCAE grade 3+ AEs[a]

TR adverse events, n (%)	Grade 3	Grade 4	Total (n=18)
Neutrophil count decrease	3 (17)	2 (11)	5 (28)
AST increase	1 (6)		1 (6)
Anaemia	1 (6)		1 (6)
Weight loss	1 (6)		1 (6)

- 4 of 18 (22%) patients had DLTs; all resumed therapy after dose reduction

Dose limiting toxicities, n (%)	Grade 3	Grade 4	Total (n=18)
Neutrophil count decrease		2 (11)	2 (11)
AST increase	1 (6)		1 (6)
Weight loss	1 (6)		1 (6)

- No surgical morbidity reported

[a] One patient had both Grade 3 neutrophil count decrease and Grade 3 weight loss

AE, adverse event; AST, aspartate aminotransferase; CTCAE, common terminology criteria for adverse events; DLT, dose-limiting toxicity

Laetsch TW, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 10008) (Oral presentation)

ADVL1823: SUMMARY

- Larotrectinib is highly active and well tolerated in newly diagnosed patients with IFS
- Larotrectinib facilitates non-morbid surgery in patients with initially unresectable IFS
- Local control remains important after larotrectinib therapy
- Ongoing follow-up will evaluate durability of response after treatment discontinuation at protocol specified response-adapted timepoints with or without surgical resection of tumour
- Late effects continue to be evaluated, including neurocognitive assessments

Clinical Perspective

- **Almost all patients treated with larotrectinib achieved a partial or complete response**
- **Local control (surgery) is important to achieve long-term results even in the case of PR or CR**
- **In the case of progression, restarting the same treatment can be beneficial**
- **Trial provides confirmation of the value of agnostic TRK fusion targets**

COG, childrens oncology group; CR, complete response; IFS, infantile fibrosarcoma; PR, partial response

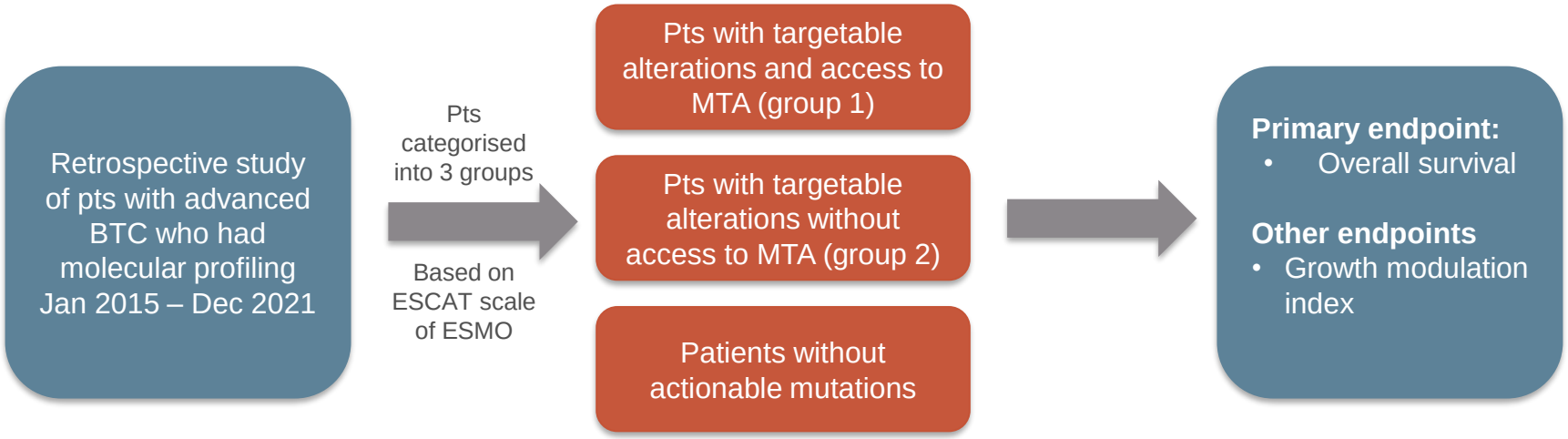
Laetsch TW, et al. J Clin Oncol. 2023;41 (suppl 16) abstr 10008) (Oral presentation)

IMPACT OF MOLECULAR PROFILING ON SURVIVAL IN PATIENTS WITH ADVANCED BILIARY TRACT CANCERS

Antoun L, et al. WCIGC 2023. Abstract #SO-4

BACKGROUND AND STUDY DESIGN

- **Biliary tract cancers (BTC) are a group of rare cancers** (intrahepatic cholangiocarcinoma [ICC], extrahepatic cholangiocarcinoma, and gallbladder carcinoma) that are epidemiologically, aetiologically, clinically, and pathologically heterogeneous
- **Due to late diagnosis, their prognosis remains poor**, and therapeutic options are limited
- **BTCs harbour distinct molecular patterns with respect to the primary tumour location**, e.g., especially ICC
- The aim was **to determine whether agents targeting molecular alterations was associated with longer overall survival compared to conventional treatments** in advanced BTC



GMI was calculated as a ratio of TTP under MTA to the TTP of the prior line of treatment; GMI ≥1.33 indicates clinically relevant benefit in group 1 vs group 2 and 3 pooled

ESCAT, ESMO scale of clinical actionability for molecular targets; ESMO, European Society of Medical Oncology; GMI, growth modulation index; pts, patients; TTP, time to progression

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RESULTS

PATIENT CHARACTERISTICS

N (%)	Group 1 TA, MTA N=77	Group 2 TA, conventional Tx N=37	Group 3 No TA N=126
Age at diagnosis			
≤65	52 (68)	22 (59)	91 (72)
>65	25 (32)	15 (41)	35 (28)
Sex			
Female	48 (62)	19 (51)	65 (52)
Male	29 (38)	18 (49)	61 (48)
Primary			
ICC	56 (73)	21 (57)	74 (59)
ECC	10 (13)	12 (32)	36 (29)
GBC	11 (14)	4 (11)	16 (13)
Stage at diagnosis			
Locally advanced	32 (42)	16 (43)	52 (41)
Metastatic	45 (58)	21 (57)	74 (59)
Treatment line			
1L or 2L	47 (61)	23 (62)	79 (63)
≥3L	30 (39)	14 (38)	47 (37)
Death status	58 (75)	33 (89)	105 (83)

MOLECULAR PROFILE

N (%)	
Patients with ESCAT alterations, N	146
Most frequent alterations (%)	
FGFR2	13
IDH1	13
ERBB2	9

EFFICACY RESULTS

	Group 1 TA, MTA N=77	Group 2 TA, conventional Tx N=37	Group 3 No TA N=126
Median OS, months	26.3	20.8	-
HR (95% CI) P-value	0.64 0.46-0.90 P=0.009	1.16 (0.78-1.72) P=0.5	-
GMI ≥1.33 (%)	49	35	32

1L/2L/3L, first/second/third line; CI, confidence interval; ECC, extrahepatic cholangiocarcinoma; ERBB2, Erb-B2 receptor tyrosine kinase 2; ESCAT, ESMO scale of clinical actionability for molecular targets; FGFR2, fibroblast growth factor receptor 2; GBC, gallbladder carcinoma; GMI, growth modulation index; HR, hazard ratio; IDH1, isocitrate dehydrogenase-1; ICC, intrahepatic cholangiocarcinoma; MTA, molecularly targeted agent; NR, not reported; OS, overall survival; TA, targetable alteration; Tx, treatment

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SUMMARY

- Identifying and categorising TAs as per ESCAT classification and administering MTAs accordingly is associated with a longer OS in patients with advanced BTC

Clinical Perspective

- **Molecular profiling by NGS to identify an actionable target(s) and treatment with a MTA provides benefit in terms of DCR, PFS and OS**
- **The study highlights the importance of conducting NGS upfront for BTC**

BTC, biliary tract cancer; ESCAT, ESMO scale of clinical actionability for molecular targets; MTA, molecularly targetable agent; OS, overall survival; TA, targetable alteration

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