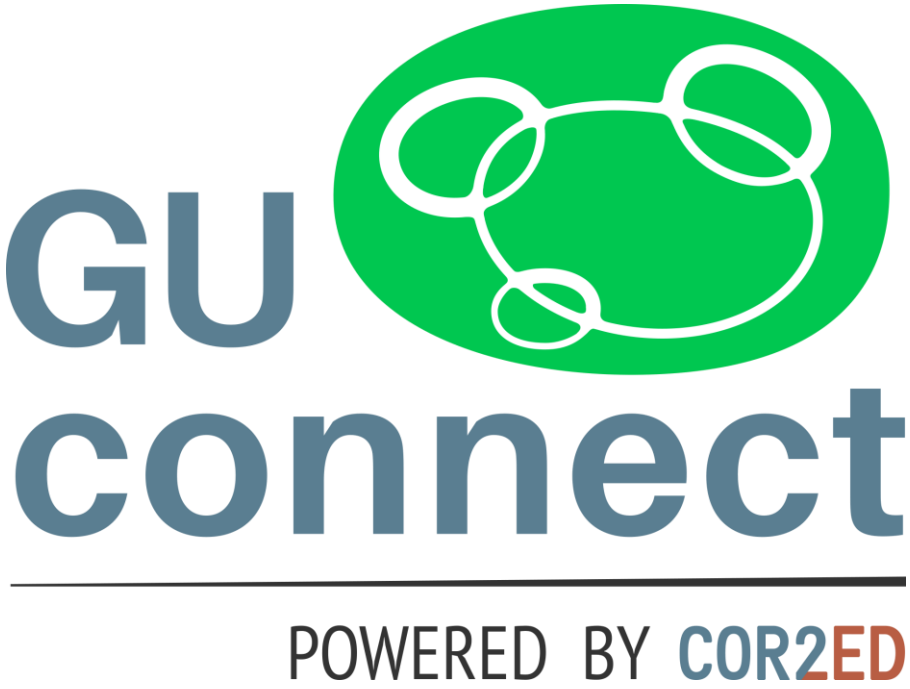
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UPDATE FROM ASCO GU FEBRUARY 2018, SAN FRANCISCO, USA

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UROTHELIAL CARCINOMA

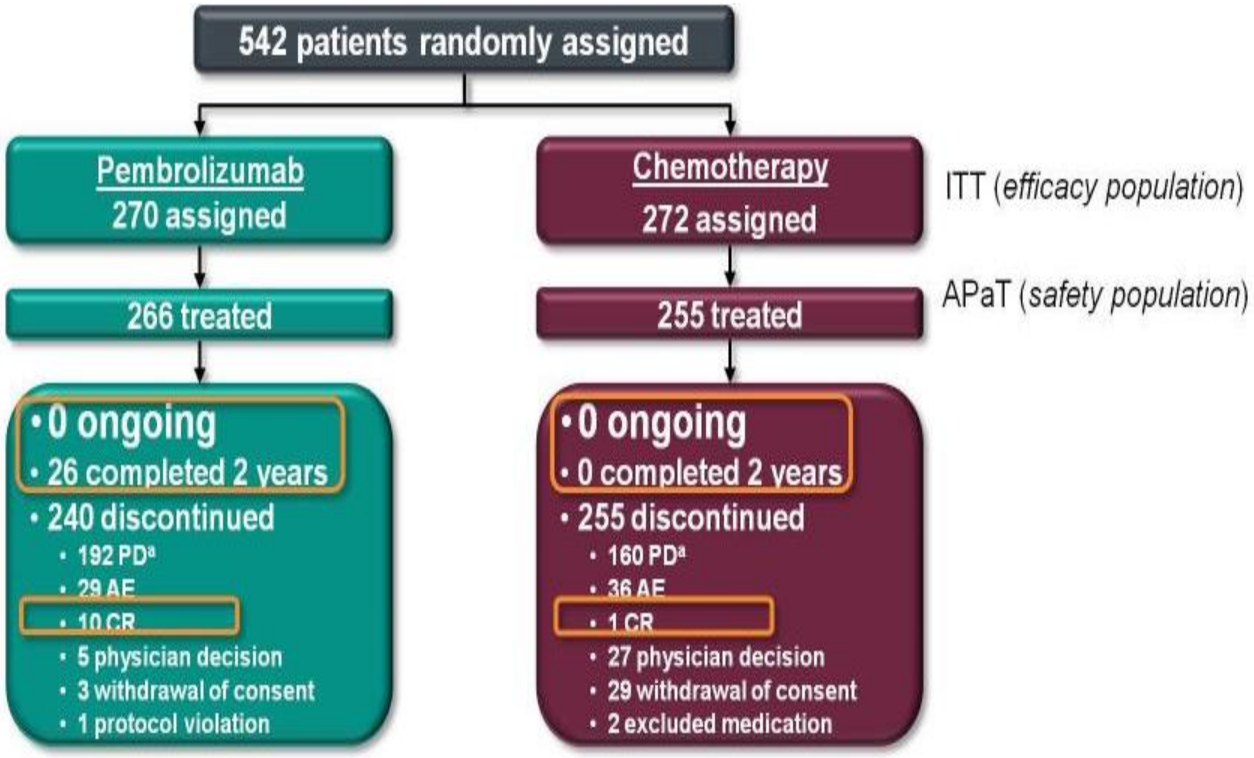
DISCLAIMER

Please note: The views expressed within this presentation are the personal opinions of the author. They do not necessarily represent the views of the author's academic institution or the rest of the GU CONNECT group

TWO-YEAR FOLLOW-UP FROM THE PHASE III KEYNOTE-045 TRIAL OF PEMBROLIZUMAB VERSUS INVESTIGATOR'S CHOICE (PACLITAXEL, DOCETAXEL, OR VINFLUNINE) IN RECURRENT, ADVANCED UROTHELIAL CANCER

Bellmunt et al. Abstract #410

KEYNOTE-045
DISPOSITION OF STUDY TREATMENTS

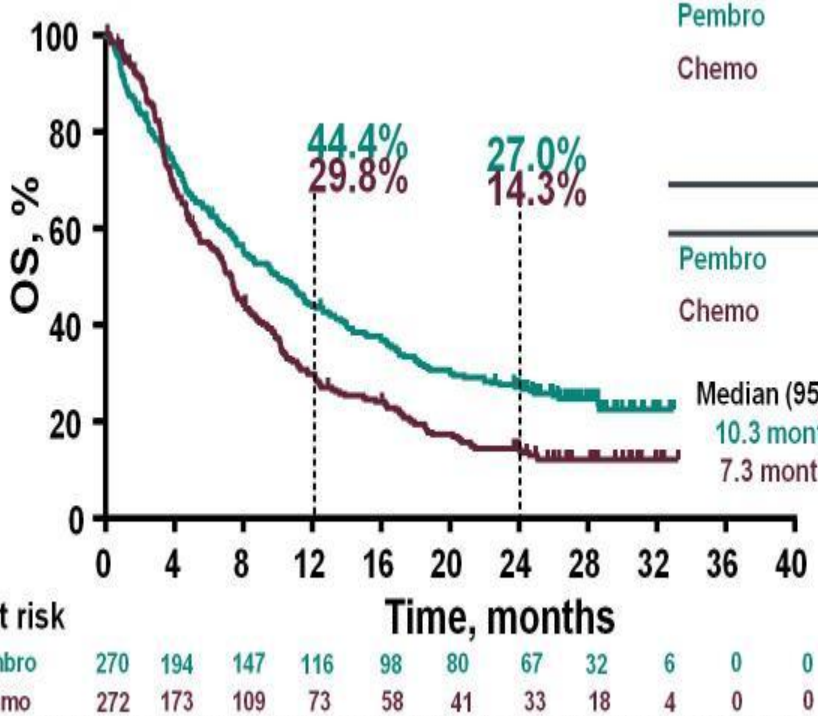


[a]Includes clinical PD.
Data cutoff date: October 26, 2017.

AE: Adverse Events; APaT: All Patients as Treated; CR: Complete Response; ITT: Intent To Treat; PD: Progressive Disease

Bellmunt et al. Abstract #410 Presented at ASCO GU 2018

KEYNOTE-045
OVERALL SURVIVAL: TOTAL



14.1 months of follow-up[1]

	Events, n	HR (95% CI)[a]	P[b]
Pembro	155	0.73 (0.59-0.91)	0.0022
Chemo	179		

27.7 months of follow-up

	Events, n	HR (95% CI)[a]	P[b]
Pembro	199	0.70 (0.57–0.85)	0.00017
Chemo	218		

Median (95% CI):
10.3 months (8.0–12.3)
7.3 months (6.1–8.1)

60.6% at 24 months in the chemotherapy arm received an immunotherapeutic agent, including those who received pembrolizumab as part of the cross over.

[a]Based on Cox regression model with treatment as a covariate stratified by ECOG performance status (0/1 vs 2), liver metastases (yes vs no), hemoglobin (<10 vs ≥10 g/dL), and time from completion of chemotherapy (<3 vs ≥3 months). [b]One-sided *P* value based on stratified log-rank test.
Data cutoff date: October 26, 2017.
1. Bellmunt J et al. *N Engl J Med*. 2017;376:1015-1026.

CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; HR: Hazard Ratio; OS: Overall Survival
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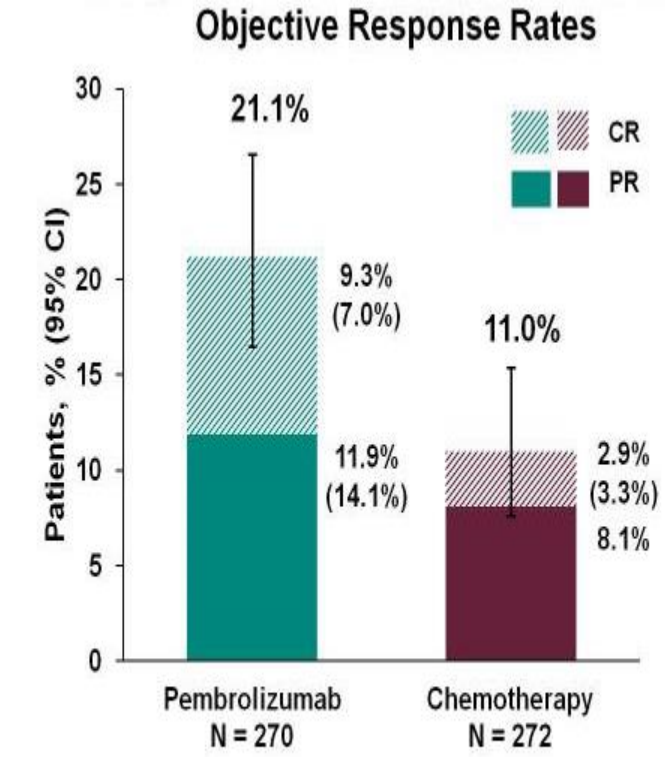
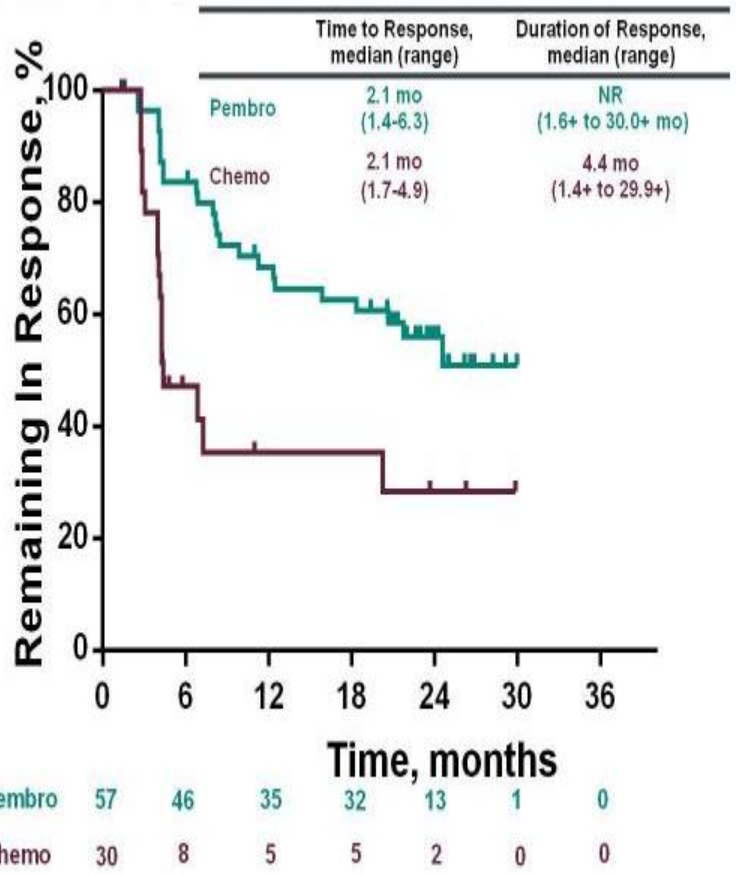
KEYNOTE-045: OBJECTIVE RESPONSE AND RESPONSE DURATION



Assessed per RECIST v1.1 by blinded, independent central review.
Data cutoff date: October 26, 2017.



	Time to Response, median (range)	Duration of Response, median (range)
Pembro	2.1 mo (1.4-6.3)	NR (1.6+ to 30.0+ mo)
Chemo	2.1 mo (1.7-4.9)	4.4 mo (1.4+ to 29.9+)

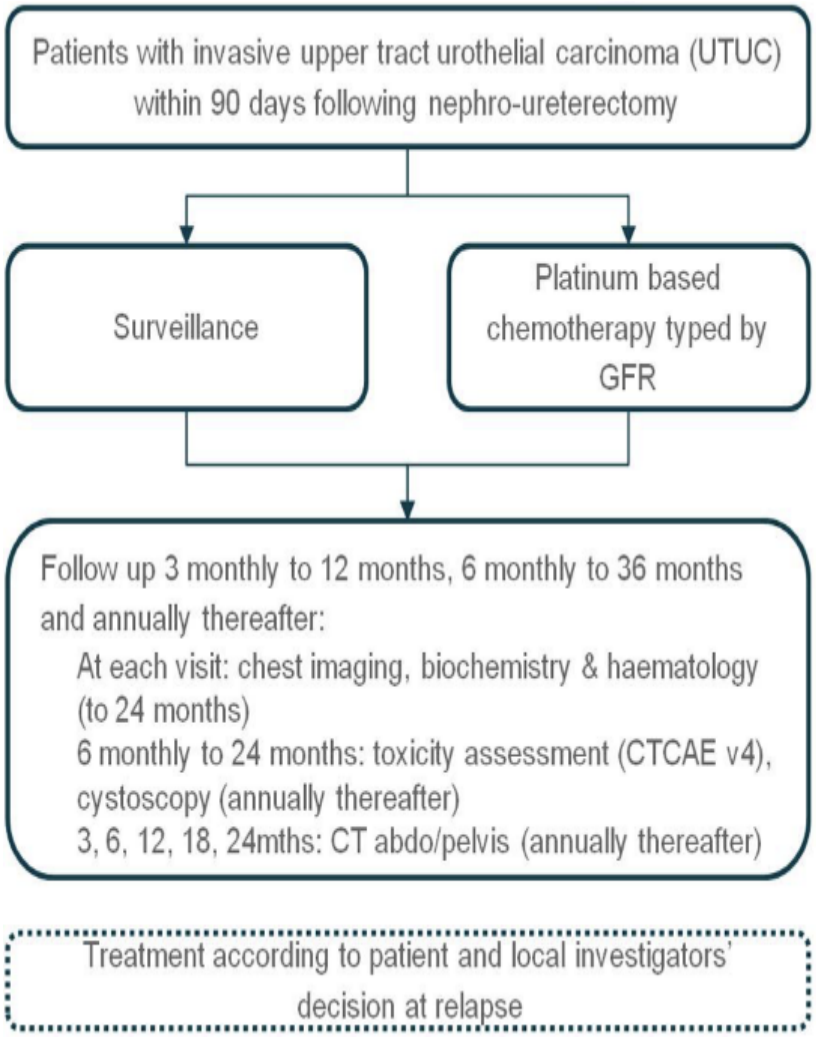
CI: Confidence Interval; CR: Complete Response; PR: Partial Response

Bellmunt et al. Abstract #410 Presented at ASCO GU 2018

RESULTS OF POUT: A PHASE III RANDOMIZED TRIAL OF PERI-OPERATIVE CHEMOTHERAPY VERSUS SURVEILLANCE IN UPPER TRACT UROTHELIAL CARCINOMA

Birtle et al. Abstract #407

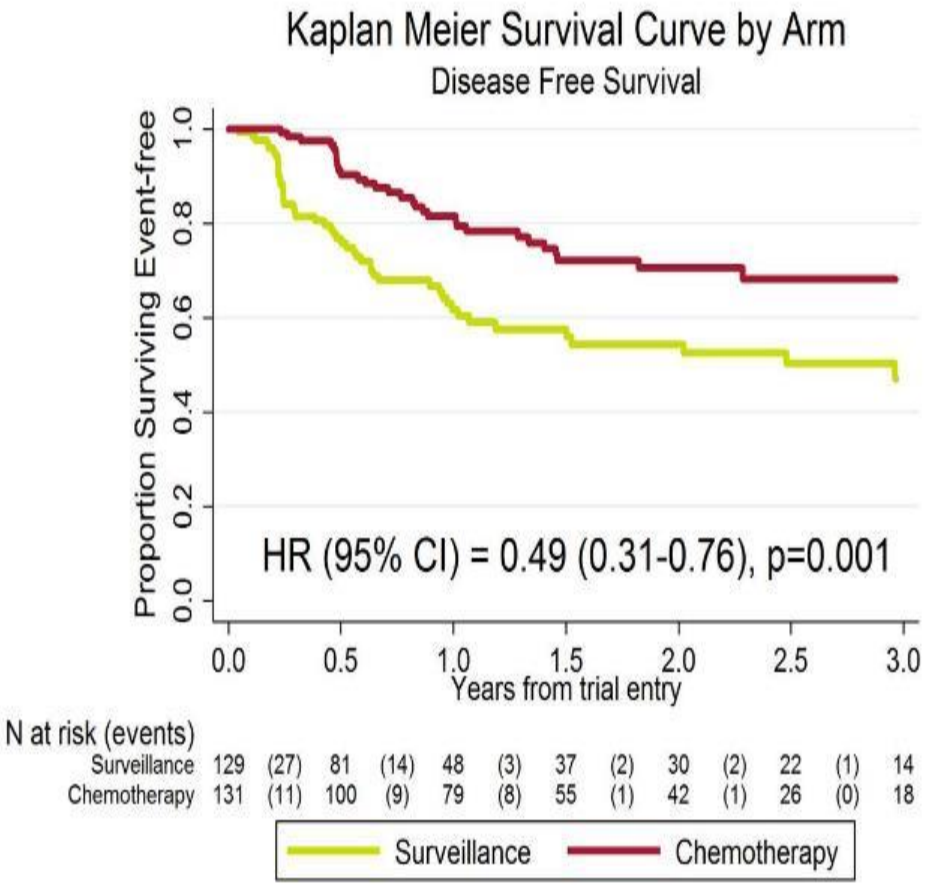
POUT TRIAL DESIGN



GFR: Glomerular Filtration Rate; CT: Computed Tomography; CTCAE: Common Terminology Criteria for Adverse Events

Birtle et al. Abstract #407 Presented at ASCO GU 2018

POUT: PRIMARY ENDPOINT – DISEASE FREE SURVIVAL



CI: Confidence Interval; HR: Hazard Ratio

Birtle et al. Abstract #407 Presented at ASCO GU 2018

POUT: CONCLUSIONS

- Adjuvant platinum-based chemotherapy improved DFS in UTUC
- POUT is the largest randomized trial in this population and chemotherapy demonstrated improved DFS compared to surveillance

DFS: Disease Free Survival; UTUC: Upper Tract Urothelial Carcinoma

Birtle et al. Abstract #407 Presented at ASCO GU 2018

ROGARATINIB TREATMENT OF PATIENTS WITH ADVANCED UROTHELIAL CARCINOMAS PRESCREENED FOR TUMOR FGFR mRNA EXPRESSION

Joerger et al. Abstract #494

BACKGROUND AND METHODS

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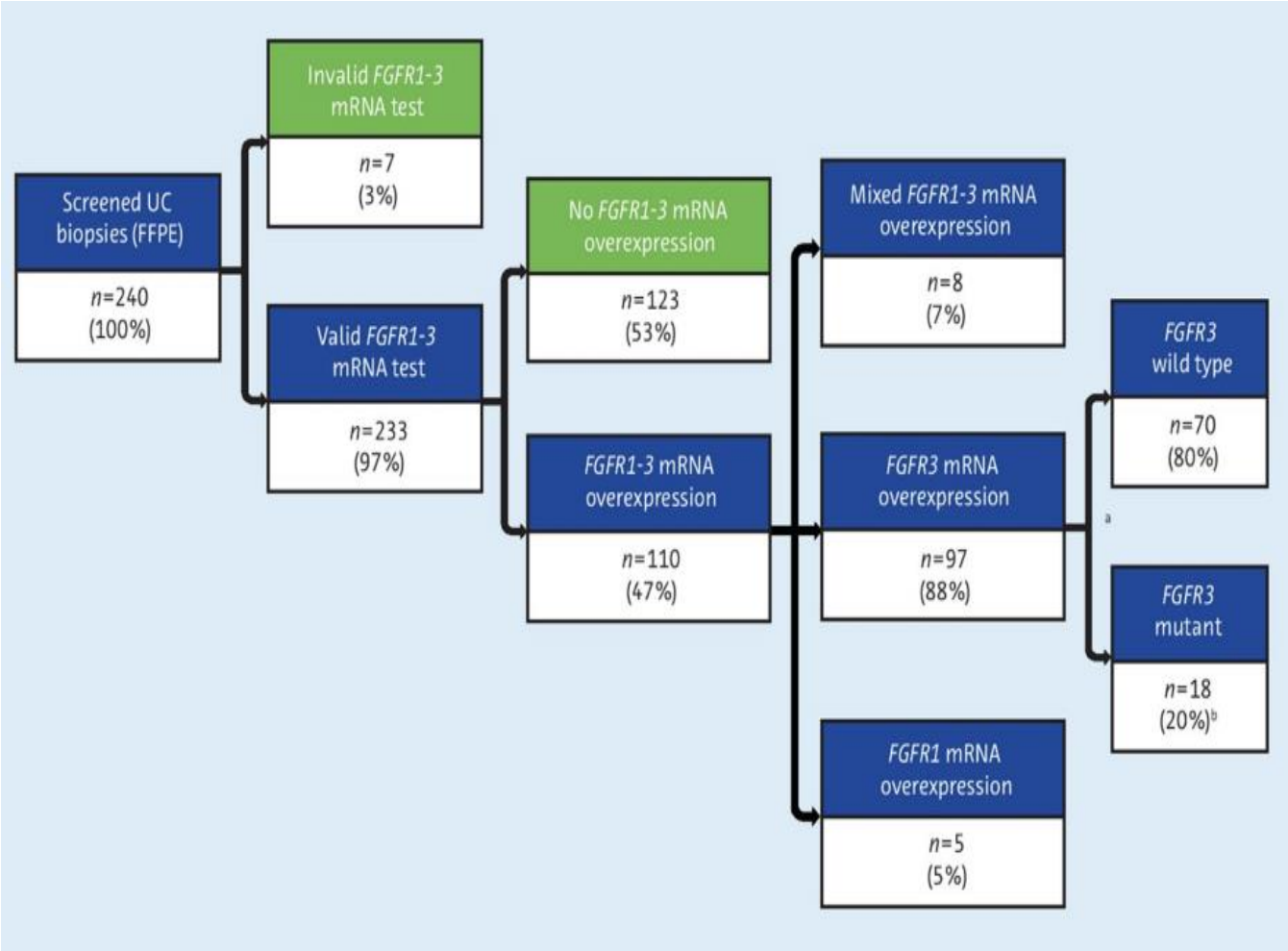
- Activation of FGFR signaling is involved in a variety of malignancies including advanced urothelial cancer (UC)
- Rogaratinib is an oral pan-FGFR kinase inhibitor
- Results from a phase I expansion cohort in UC patients prescreened for FGFR1-3 mRNA expression levels and activating mutations were reported (NCT01976741)
- Patients with advanced UC with high FGFR1-3 mRNA expression in biopsy specimens were treated with rogaratinib 800mg twice daily until tumour progression, intolerable toxicity, or withdrawal

FGFR: Fibroblast Growth Factor Receptors; UC: Urothelial Cancer; mRNA: Messenger RNA

Joerger et al. Abstract #494 Presented at ASCO GU 2018

RESULTS

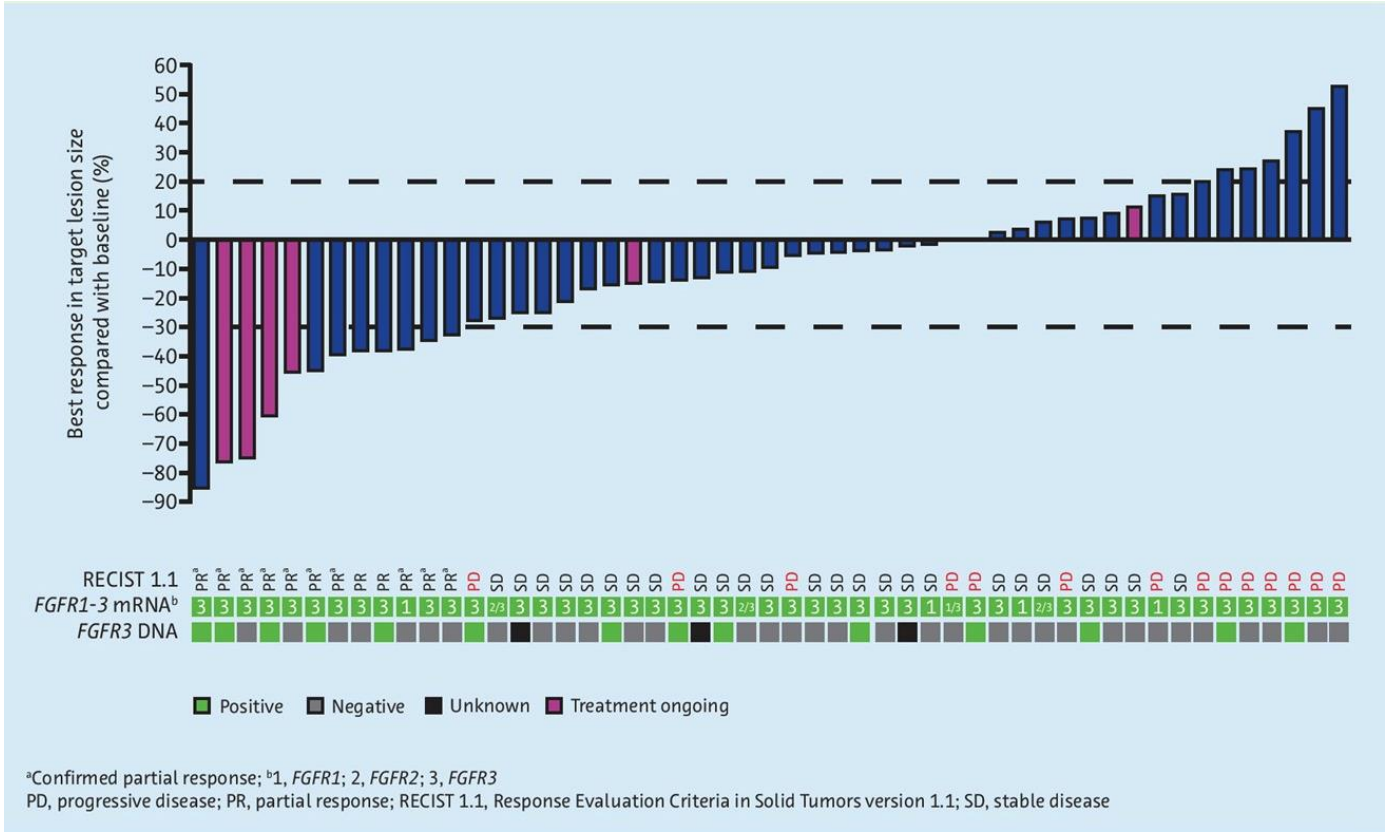


47% of UC samples showed overexpression of at least 1 *FGFR (FGFR1-3);* all FGFR3 mutant patients had in parallel high FGFR3 mRNA levels

FFPE: Formalin-fixed Paraffin-embedded; FGFR: Fibroblast Growth Factor Receptors; UC: Urothelial Cancer; mRNA: Messenger RNA

Joerger et al. Abstract #494 Presented at ASCO GU 2018

RESULTS



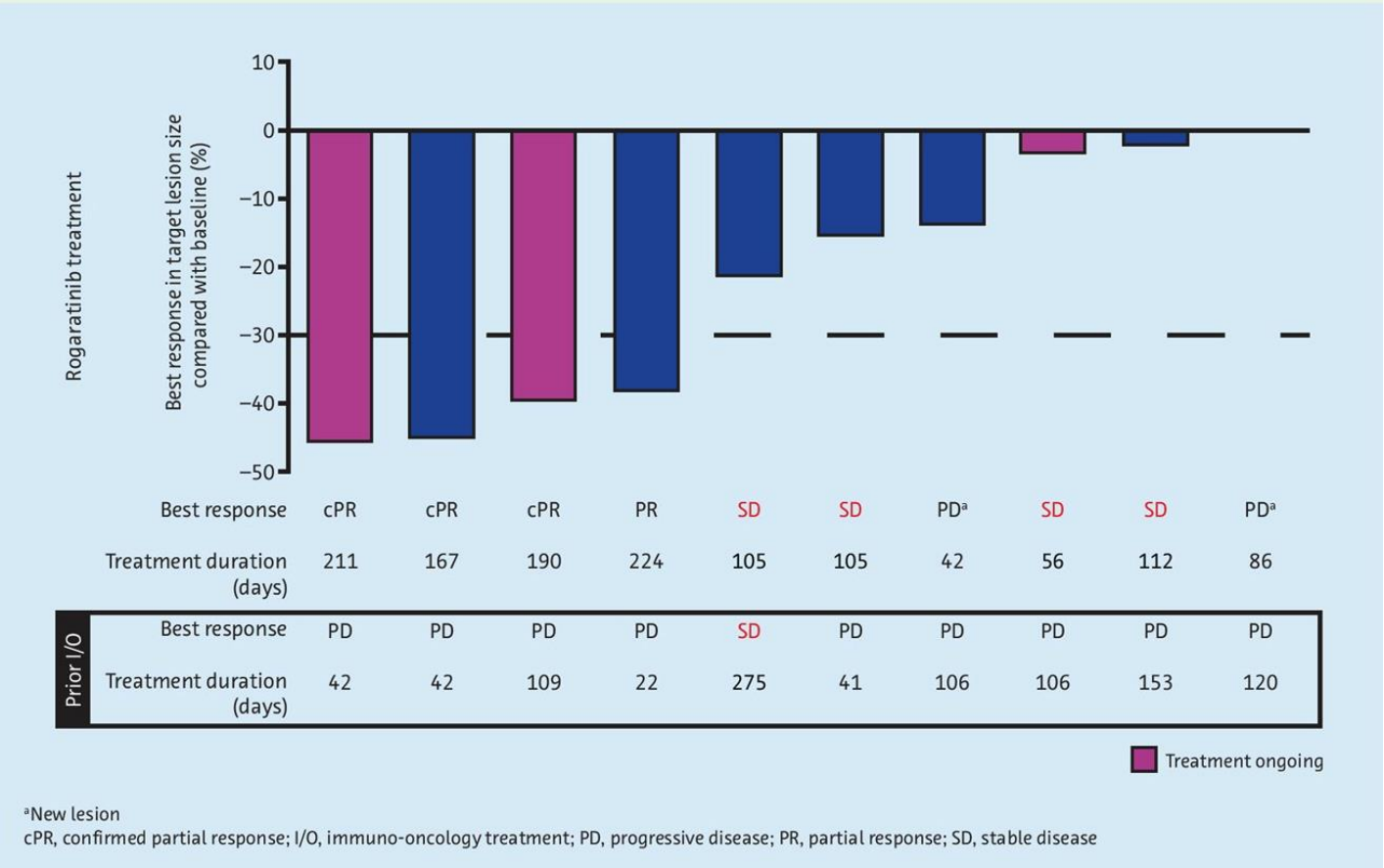
[a]Confirmed partial response; [b]1, *FGFR1*; 2, *FGFR2*; 3, *FGFR3*
PD, progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SD, stable disease

- 24% partial response to rogaratinib treatment in UC samples overexpressing *FGFR1-3* mRNA
- 64% with partial response and 80% with stable disease showed *FGFR3* mRNA overexpression without *FGFR3* gene mutations or translocations

FGFR: Fibroblast Growth Factor Receptors; mRNA: Messenger RNA; PD: Progressive Disease; PR: Partial Response; RECIST 1.1; Response Evaluation Criteria in Solid Tumors version 1.1; SD: Stable Disease

Joerger et al. Abstract #494 Presented at ASCO GU 2018

RESULTS



FGFR-positive patients enrolled on rogaratinib had low benefit from prior I/O treatment

[a]New lesion

FGFR: Fibroblast Growth Factor Receptors; cPR: confirmed partial response; I/O: immuno-oncology treatment; PD: progressive disease; SD: stable disease

Joerger et al. Abstract #494 Presented at ASCO GU 2018

CONCLUSIONS

- Selection of patients for treatment with rogaratinib based on FGFR mRNA expression levels was feasible and identified drug-sensitive patients with and without underlying DNA alterations

- Rogaratinib had a favorable safety profile and showed promising anti-tumor activity in UC patients, including those refractory to prior I/O treatment

FGFR: Fibroblast Growth Factor Receptors; I/O: Immuno-oncology treatment; mRNA: Messenger RNA; UC: Urothelial Cancer

Joerger et al. Abstract #494

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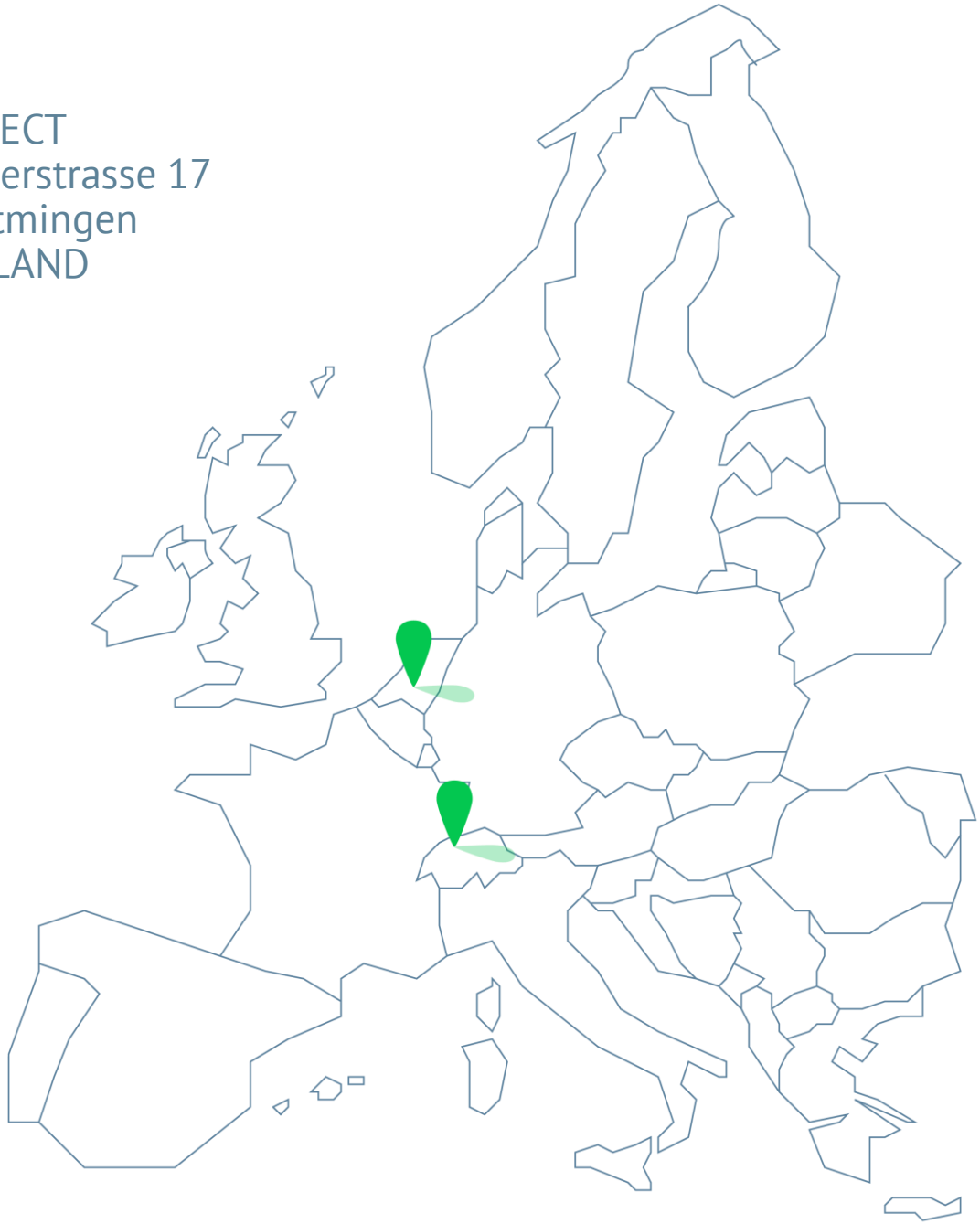

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