Cetuximab in Patients with Breast Cancer and Non-Small Cell Lung Cancer without reported *KRAS, NRAS, BRAF* Mutations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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Background

- The TAPUR Study is a phase II basket study that evaluates the anti-tumor activity of commercially available targeted agents used in patients (pts) with advanced cancers with genomic alterations that are known targets for drugs in TAPUR.
- Results in two cohorts of pts with 1) breast cancer (BC) and 2) non-small cell lung cancer (NSCLC) without reported *KRAS, NRAS, BRAF* mutations treated with cetuximab are reported.

Methods

Study Design:

- Eligible pts had advanced BC or NSCLC with no remaining standard treatment options, PS 0-2, and adequate organ function. Treatment was assigned according to pre-specified protocol matching rules based on genomic testing performed using commercially available tests selected by clinical sites.
- All pts in this analysis had advanced BC or NSCLC without reported *KRAS, NRAF, BRAF* mutations.
- Pts received cetuximab (C) as an initial intravenous infusion of 400 mg/m^2 over 120 minutes and subsequent weekly infusions of 250 mg/m^2 over 60 minutes until disease progression. Tumor evaluations were performed at weeks (wks) 8 and 16 after treatment initiation.
- Primary endpoint is objective response (OR) at or before 16 wks or stable disease (SD) ≥ 16 wks per RECIST v1.1. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and toxicity per CTCAE. Grades 3-4 adverse events (AEs) at least possibly related to drug are reported.

Statistical methods:

- Simon's optimal two stage design was used to test the null hypothesis of 15% response rate versus the alternative of 35%.
- Power and one-sided type I error rate were set at 85% and 10%, respectively.
- Design requires 10 pts in stage 1 and if <2 pts have OR at or before 16 wks or SD ≥ 16 wks, the cohort is closed.

Results

Table 1: Demographics and Baseline Characteristics

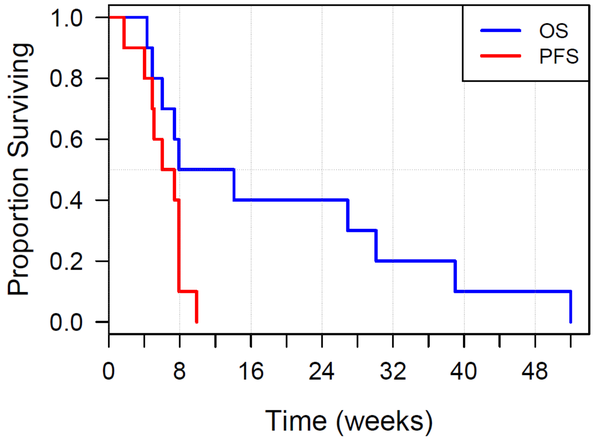
Characteristic	Cetuximab without reported *KRAS, NRAS, BRAF* mutations, N (%)	
Tumor Type	BC (N=10)	NSCLC (N=10)
Median Age, years (range)	59 (45-65)	60 (55-82)
Sex		
Male	0 (0%)	6 (60%)
Race		
White	6 (60%)	8 (80%)
African-American	3 (30%)	1 (10%)
Other	1 (10%)	1 (10%)
ECOG Performance Status		
0	6 (60%)	1 (10%)
1	3 (30%)	9 (90%)
2	1 (10%)	0 (0%)
Prior Treatments		
Pts with radiation therapy	9 (90%)	7 (70%)
Pts with prior systemic therapies		
1	1 (10%)	0 (0%)
2	1 (10%)	2 (20%)
3	8 (80%)	8 (80%)
Genomic Test Performed		
FoundationOne	5 (50%)	7 (70%)
Caris MIProfile	4 (40%)	3 (30%)
Other	1 (10%)	0 (0%)

- Baseline demographics and clinical characteristics are shown in Table 1.

Clinical Outcomes

- No ORs at or before 16 wks or SD ≥ 16 wks were observed in the BC or NSCLC pts and both cohorts were therefore closed at the end of stage 1. A single grade 3 AE of hypomagnesemia was reported in the NSCLC cohort as possibly related to C.

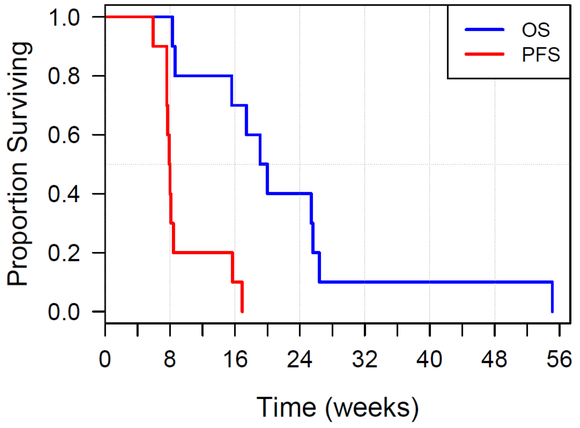
Figure 1: OS and PFS in Advanced BC Pts treated with Cetuximab without reported *KRAS, NRAS, BRAF* Mutations



Advanced BC Pts (see Figure 1)

- 10 pts were enrolled from June 2016 to May 2018.
- mPFS, wks, (90% CI) : 6.7 (4.0, 7.9)
- mOS, wks, (90%CI) : 11.0 (4.9, 30.1)
- No grade 3, 4 or 5 AEs or SAEs reported as at least possibly related to C.

Figure 2: OS and PFS in Advanced NSCLC Pts treated with Cetuximab without reported *KRAS, NRAS, BRAF* Mutations



Advanced NSCLC Pts (see Figure 2)

- 10 pts were enrolled from January 2017 to May 2018.
- mPFS, wks, (90% CI) : 8.0 (7.6, 8.4)
- mOS, wks, (90%CI) : 19.6 (8.6, 25.6)
- A single grade 3 AE of hypomagnesemia was reported in the NSCLC cohort as possibly related to C.

Conclusions

These results suggest monotherapy with C does not have clinical activity in pts with advanced breast or non-small cell lung cancer without reported *KRAS, NRAS BRAF* mutations. Other treatments should be considered for these pts, including treatments offered in clinical trials.

Acknowledgments

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