Abstract 3131: Afatinib in patients with solid tumors with neuregulin 1 (*NRG1*) fusions: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

ASCO TAPUR
Targeted Agent and Profiling Utilization Registry Study

J Rodon[1], M Rothe[2], PK Mangat[2], E Garrett-Mayer[2], TL Cannon[3], E Hobbs[4], G Kalemkerian[5], DC Hinshaw[2], A Gregory[2], GN Grantham[2], S Halabi[6], RL Schilsky[2]

[1]Department of Investigational Cancer Therapeutics, University of Texas MD Anderson Cancer Center, Houston, TX; [2]American Society of Clinical Oncology, Alexandria, VA; [3]Inova Schar Cancer Institute, Fairfax, VA; [4]Providence Cancer Institute, Portland, OR; [5]University of Michigan, Ann Arbor, MI; [6]Duke University Medical Center, Durham, NC

ASCO
AMERICAN SOCIETY OF CLINICAL ONCOLOGY

Background:

- TAPUR is a phase II basket study that evaluates antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Prior studies demonstrated promising clinical benefit of afatinib, an EGFR TKI, in pts with lung, pancreatic, or colorectal cancers (CRC) with *NRG1* fusions [1-3].
- **Results of a small cohort of pts with various solid tumors with *NRG1* fusions treated with afatinib are reported.**

Methods:

Study Design:

- **Eligible pts:** Advanced solid tumors harboring a *NRG1* fusion, ECOG performance status (PS) 0-2, adequate organ function, measurable disease, and no standard treatment (tx) options. Pts with non-small cell lung cancer (NSCLC) were eligible if they did not have pathogenic mutations in *ALK, BRAF, EGFR* or *ROS1*. Tx was assigned according to prespecified matching rules based on genomic tests performed in CLIA-certified, CAP-accredited laboratories selected by sites.
- Pts received a 40 mg tablet of afatinib daily until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- **Primary endpoint:** Disease control (DC) defined by investigator assessment of objective response (OR) or stable disease (SD) of at least 16+ weeks (wks) duration (SD16+) per RECIST v1.1. Radiographic confirmation of response was not required.
- **Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response (DOR), duration of SD, and Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) per CTCAE v4.0 at least possibly related to tx are reported. DOR is defined as time from pt's first documented OR to progressive disease (PD). Duration of SD is defined as time from tx start to PD.
- This cohort was closed after 2 years before completing stage 1 enrollment (planned n=10) according to a prespecified cohort closure rule.

Results:

- 4 pts were enrolled from February 2020 to July 2021. Patient characteristics are outlined in **Table 1.**
- **Outcomes**: 3 pts (75%) had DC: PR (1) and SD16+ (2). DOR was 24 wks and durations of SD for the pts with SD16+ were 64 and 134 wks (**Table 2**). The pt with SD16+ and CRC underwent resection of a remaining target lesion in September 2022 and is still alive off study at 212 wks as of March 2024.
- **Safety:** No grade 3-5 tx-related AEs or SAEs were reported.

The authors thank the patients who participated in this cohort, and the clinical centers and staff. The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). This was an independent, investigator-initiated study supported by Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI). BIPI had no role in the design, analysis, or interpretation of the results in this study. BIPI was given the opportunity to review the poster for medical and scientific accuracy as it relates to BI substances, as well as intellectual property considerations.

Contact: TAPURPublications@asco.org

Conclusion: Though a small sample size, afatinib demonstrated prolonged disease control in some patients with solid tumors with a *NRG1* fusion.

Future Direction: Additional study in a larger group of patients is warranted to confirm the efficacy of afatinib in this patient population.

Table 1. Clinical Characteristics, Tumor Origin, Alterations, and Best Response for All Pts (N=4)

Clinical Characteristics	Best Response	Primary Tumor Origin	Time to progression, wks	*NRG1* fusion	Co-alterations[a]
58-year-old White, non-Hispanic female, ECOG PS 0, 2 prior systemic therapies	PR	NSCLC	32	*NRG1-CD74* fusion	*CCNE1* amp *GATA6* amp-equivocal *TP53* R65fs*58 *ALK* G1121D[b] *C17ORF39* H131Q[b] *CDKN2A/B* p16INK4a A4OS[b] *DDR1* amp[b] *FANCC* E273K[b] *INPP4B* A757G[b] *MST1R* rearrangement[b] *NOTCH1* G2259A[b] *P2RY8* V313L[b] *RICTOR* I1601V[b], R907C[b] *TBX3* H36Y[b]
47-year-old White, Hispanic female, ECOG PS 1, 3 prior systemic therapies	SD16+	CRC	N/A[c]	*NRG1-MATN2* fusion	*APC* Q1367* *DDX11* A769fs*11 *FBXW7* S678* *FGFR1* copy number gain *TP53* A76fs*55 *MSH2* A54T[b] *TRAF7* G182R[b]
49-year-old Black, non-Hispanic male, ECOG PS 1, 5 prior systemic therapies	SD16+	Pancreas	64	*NRG1*-Exon 2 fusion	*ARID1A* G2087R
70-year-old White, non-Hispanic female, ECOG PS 0, 1 prior systemic therapy	PD	CRC	8	*NRG1-CD74* fusion	*ARID1A* Q1327* *PBRM1* W1132* *TP53* I195T *CSF3R* L23R[b] *KDM5C* R1435C[b] *TIPARP* V609I[b]

[a] No *ERBB1 (EGFR), HER2 (ERBB2), HER4 (ERBB4)* alterations were reported.
[b] Variant of unknown significance
[c] Pt underwent resection of a remaining target lesion on September 14, 2022, and has still not progressed as of March 2024.

Table 2: Efficacy Outcomes (N=4)

Median PFS, wks (95% CI)	48 (8, inf)
Median OS, wks (95% CI)	81 (35, inf)
DOR, wks (n=1)	24
Duration of SD in pts with SD16+, wks (n=2)	64 and 134

Figure 1: Percent Change in Tumor Burden Over Time (N=4)

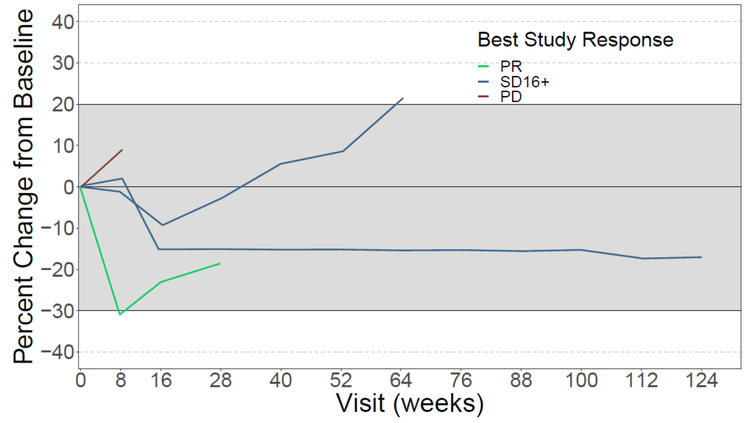
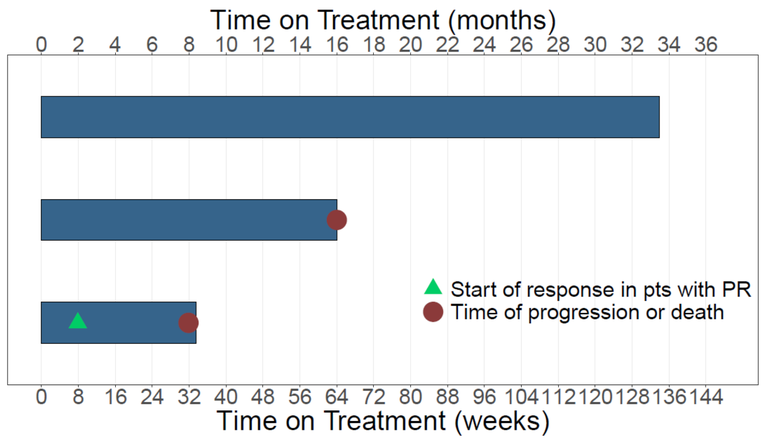


Figure 2: Time on Treatment in Pts with OR or SD16+ (n=3)



References
[1] Cadranel J, Liu SV, Duruisseaux M,... Renouf DJ. Therapeutic Potential of Afatinib in NRG1 Fusion-Driven Solid Tumors: A Case Series. Oncologist. 2021
[2] Jones MR, Williamson LM, Topham JT,... Renouf DJ. *NRG1* Gene Fusions Are Recurrent, Clinically Actionable Gene Rearrangements in *KRAS* Wild-Type Pancreatic Ductal Adenocarcinoma. Clin Cancer Res. 2019
[3] Gay ND, Wang Y, Beadling C,... Tolba K. Durable Response to Afatinib in Lung Adenocarcinoma Harboring NRG1 Gene Fusions. J Thorac Oncol. 2017