

***Phase 2 Study of Ganetespib (STA-9090)
in Subjects with Stage IIIB or IV Non-Small
Cell Lung Cancer – A Preliminary Report***

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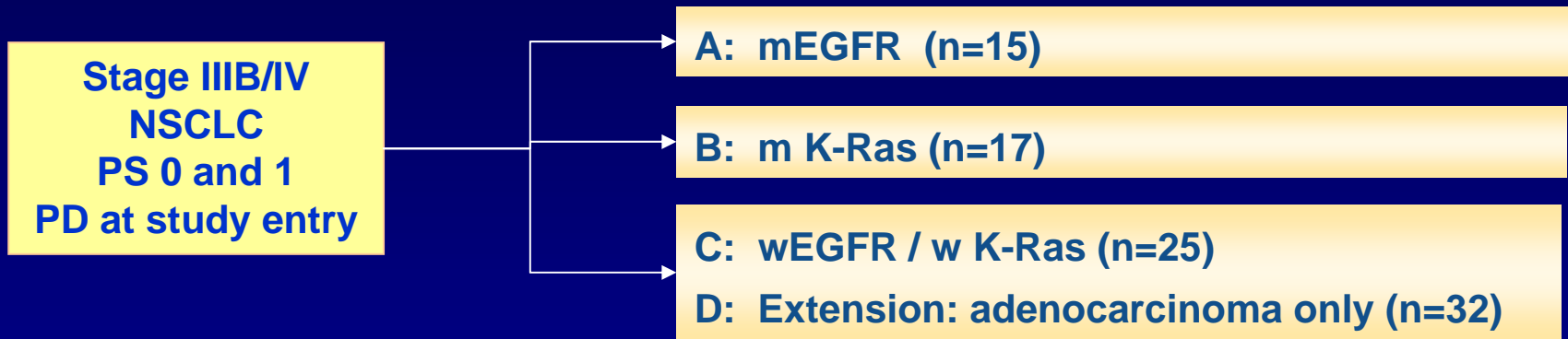


Ganetespib (STA-9090) Background

- Potent Hsp90 inhibitor, structurally unrelated to first-generation ansamycin class of Hsp90 inhibitors
 - Superior activity to these agents in preclinical studies
 - Potent activity multiple NSCLC models, single agent/combo
- Promising single-agent antitumor activity seen in early clinical trials, multiple cancers
- Well-tolerated to date, >350 patients treated, 15 trials
 - Most common AE: diarrhea; generally Grade 1 and 2, manageable with supportive care
- Absence of serious liver or common ocular toxicities seen with other Hsp90i

Study Design

**Ganetespiib at 200 mg/m² qW for 3 wks, 1 wk off
Until disease progression**



- Genotyping required for all patients
- Primary endpoint : PFS at 16 wks
- Two stage design: for cohorts A,B,C: Stage 1 (n=14 pts); if ≥ 2 pts progression-free at week 16, enroll Stage 2 (n = 9 pts)
- Patients who progressed on single agent but had some clinical benefit were allowed to roll over to cohort E: weekly ganetespiib + docetaxel (n=5)

Analysis Population: Cohort C & D

- Evaluable patients for clinical activity (N = 33)
 - Adenocarcinoma patients with wild-type EGFR & K-ras
 - Met main inclusion / exclusion criteria
 - Received at least one dose of study drug
 - Had both baseline and at least one follow-up radiological assessment
- Safety population (N = 36)
 - All adenocarcinoma patients with wild-type EGFR & K-ras who received at least one dose of study drug

Demographics and Baseline Status

		N=36
Age (yrs)	Median (Range)	59 36- 82
Sex (N, %)	Male Female	19 (52.8) 17 (47.2)
ECOG Status (N,%)	0 1 Unknown	10 (27.8) 24 (66.7) 2 (5.5)
# Prior Treatments	Mean Median (Range)	3 2 1 - 10

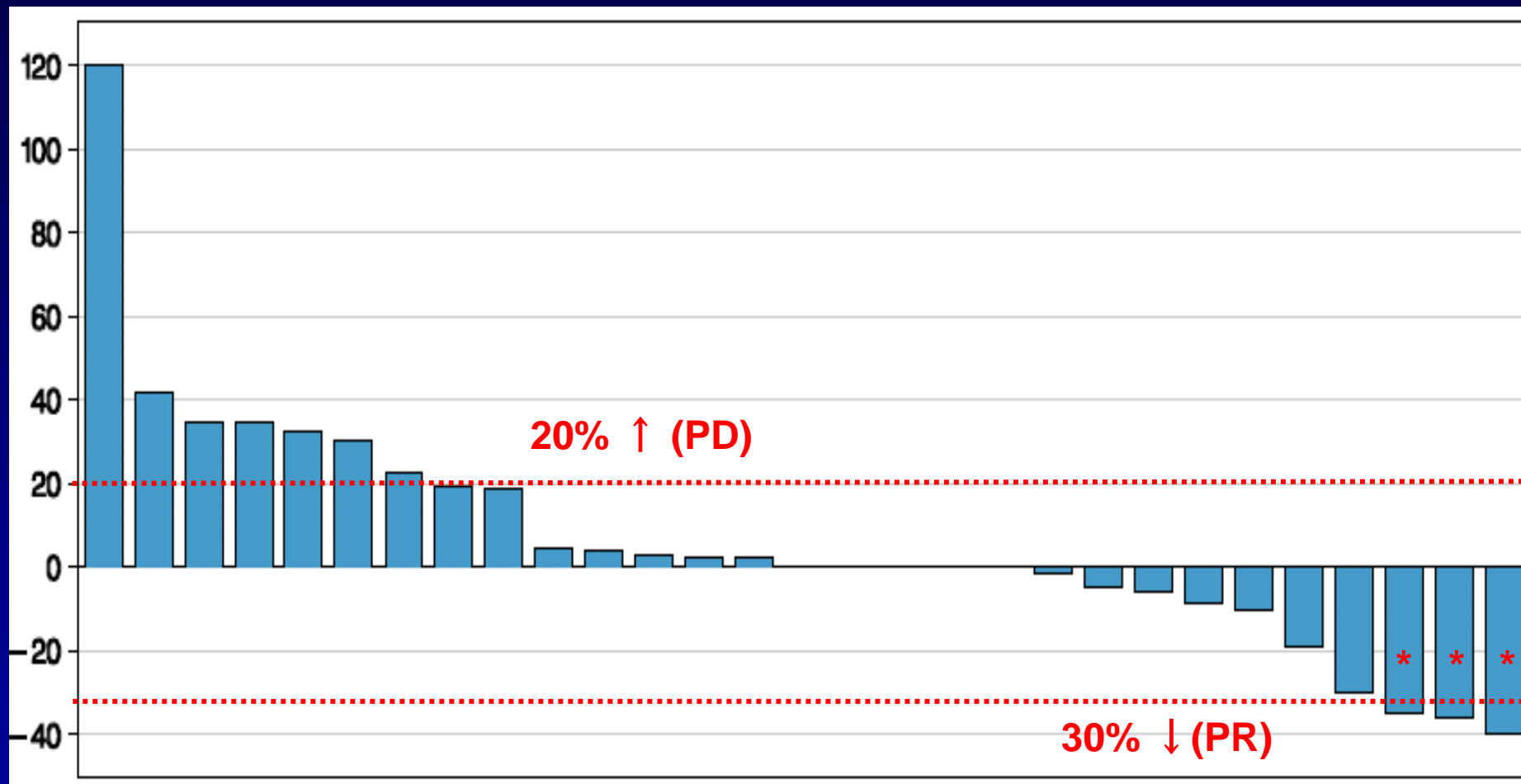
Most Common AEs

	AEs N (%) N=36	≥ Grade 3 AEs N (%) N=36
Diarrhea	31 (86)	2 (6)
Fatigue	16 (44)	4 (11)
Nausea	12 (33)	0
Decreased appetite	10 (28)	0
Insomnia	9 (25)	2 (6)
Constipation	7 (20)	0
Hyponatremia	6 (17)	3 (8)
Increased ALT	5 (14)	1 (3)
Increased Alk Phos	5 (14)	0
Increased amylase	5 (14)	3 (8)
Cough	5 (14)	0
Dyspnea	5 (14)	4 (11)
Rash	5 (14)	0
UTI	5 (14)	0

Treatment-related AEs occurring in $\geq 10\%$ of patients

	AEs N (%) N=36	\geq Grade 3 AEs N (%) N=36
Diarrhea	29 (81)	2 (6)
Fatigue	11 (31)	3 (8)
Nausea	11 (31)	0
Insomnia	6 (17)	2 (6)
Increased Alk Phos	5 (14)	0
Decreased appetite	5 (14)	0

Best change sum of longest diameters

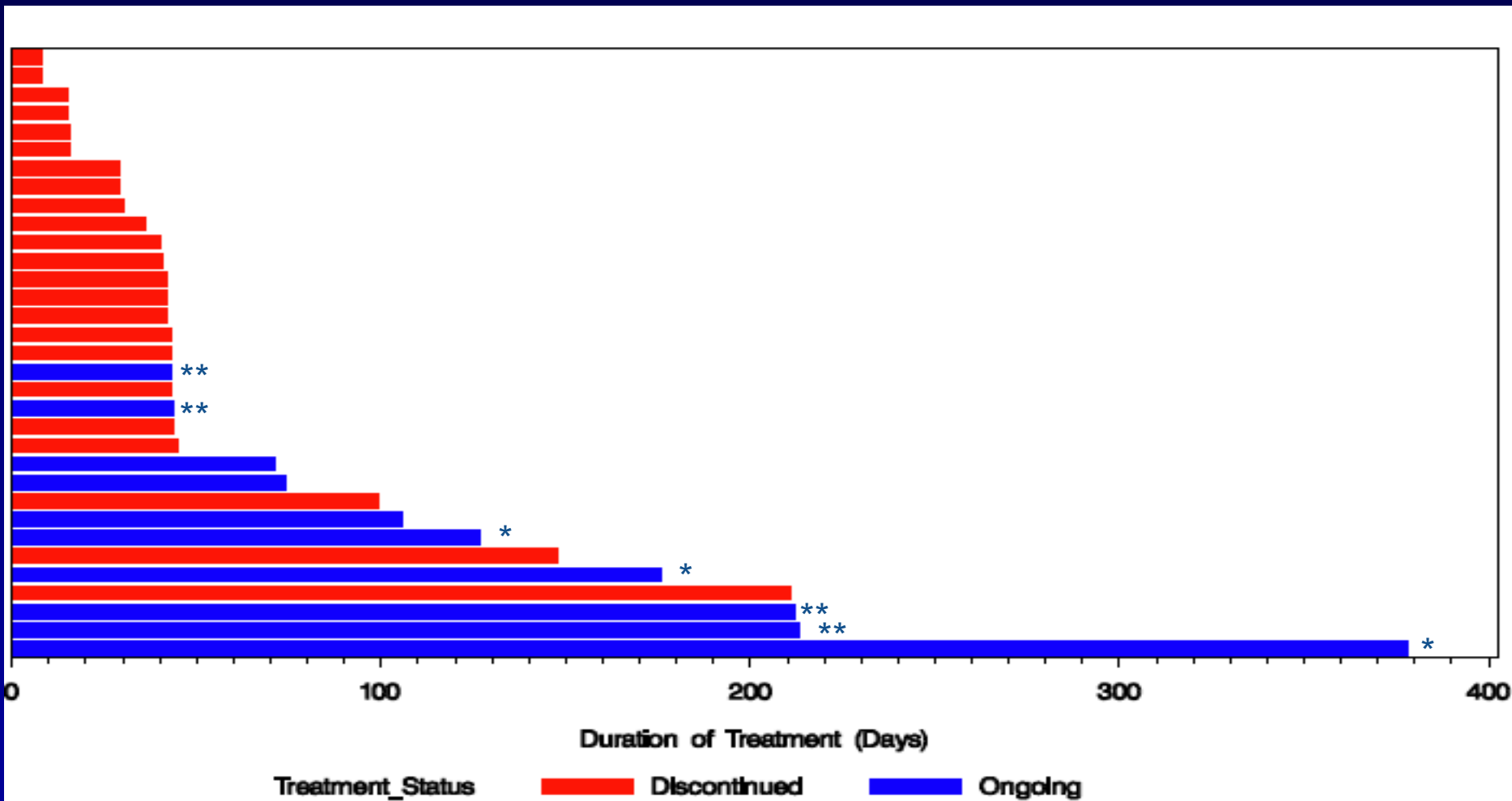


22 pts target lesion stabilization (<20%)

10 pts target lesion shrinkage

3 confirmed PRs – durable: 1 at 14 months, 2 at 6 months – all 3 ongoing

Time on treatment



- * Confirmed PRs
- ** Continued treatment on combination (Cohort E)

Dates based on last entry into database (Dec/Jan); actual duration of PRs 6, 6, 14 mos

Conclusions

- Ganetespib once weekly is well-tolerated in advanced NSCLC patients
 - Most common AE: diarrhea; generally Grade 1 and 2, manageable with supportive care
- Absence of serious liver or common ocular toxicities seen with other Hsp90i
- Clinically active as single agent
- Phase 2b/3 NSCLC trial in combination with docetaxel initiating by mid-year
 - Exploit both single-agent and chemo-sensitizing effects of Hsp90i

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