Genomic analysis of circulating tumor DNA from patients with hormone receptor-positive, *HER2*-mutant metastatic breast cancer enrolled in SUMMIT: Mechanisms of acquired resistance to neratinib + fulvestrant + trastuzumab

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#PD17-01

Introduction

Figure 1. SUMMIT study design: HR+, HER2–, *HER2*-mutant MBC cohorts

Objectives

Methods

Analysis cohort

Results

Table 1. Efficacy summary overall and according to treatment received

Parameter	Non-randomized + Randomized N+F+T Prior CDK4/6i	Randomized F+T Prior CDK4/6i	After crossover from F+T to N+F+T (n=4)	Randomized F Prior CDK4/6i	After crossover from F to N+F+T (n=4)
Objective response (confirmed CR or PR), n (%)	[illegible]	0	[illegible]	0	[illegible]
CR	[illegible]	0	0	0	0
PR	[illegible]	0	[illegible]	0	[illegible]
Best overall response (confirmed or unconfirmed PR or CR), n (%)	[illegible]	0	[illegible]	0	[illegible]
Median DOR, months (95% CI)	[illegible]	No responses	[illegible]	No responses	[illegible]
Clinical benefit, n (%)	[illegible]	0	[illegible]	0	[illegible]
Median PFS, months (95% CI)	[illegible]	[illegible]	[illegible]	[illegible]	NR

Figure 2. ctDNA samples for central NGS

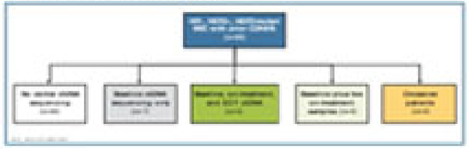


Table 2. Concordance between enrollment assay and central pretreatment ctDNA NGS

Central NGS	Enrollment assay sample type	
	FFPE tissue	ctDNA
HER2 mutation detected	[illegible]	[illegible]
HER2 mutation not detected	[illegible]	[illegible]

Figure 3. Genomic spectrum of centrally assessed ctDNA at baseline (n=24)

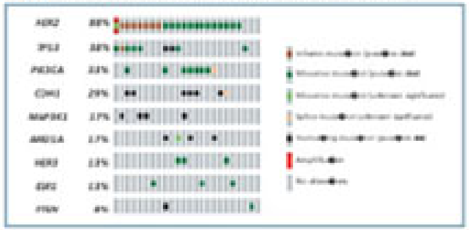
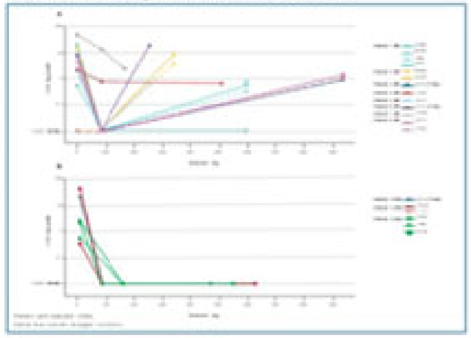


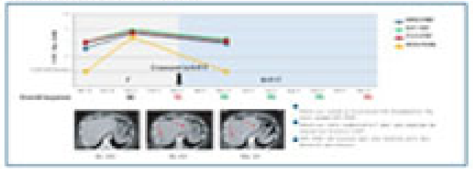
Figure 4. *HER2* mutations: VAF in patients treated with N+F+T. Blood draw and ctDNA sequencing A) at pretreatment, on-treatment, and at time of progression in patients who progressed after treatment and B) at pretreatment, on-treatment, and at last blood draw in patients who remained on treatment



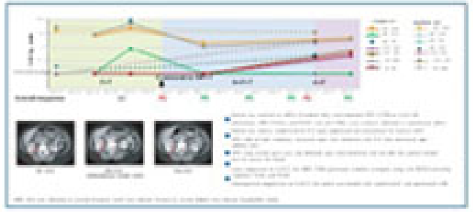
HER2 mutations in patients treated with N+F+T

Figure 5. Emergent mutations at progression on N+F+T

Crossover case study 1: F to N+F+T



Crossover case study 2: F+T to N+F+T



Conclusions

References

Acknowledgments and disclosures

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