Intratumoral CD40 Agonist (APX005M) in Combination with Pembrolizumab Induces Broad Innate and Adaptive Immune Activation in Local and Distant Tumors in CPI Treatment Naïve Metastatic Melanoma

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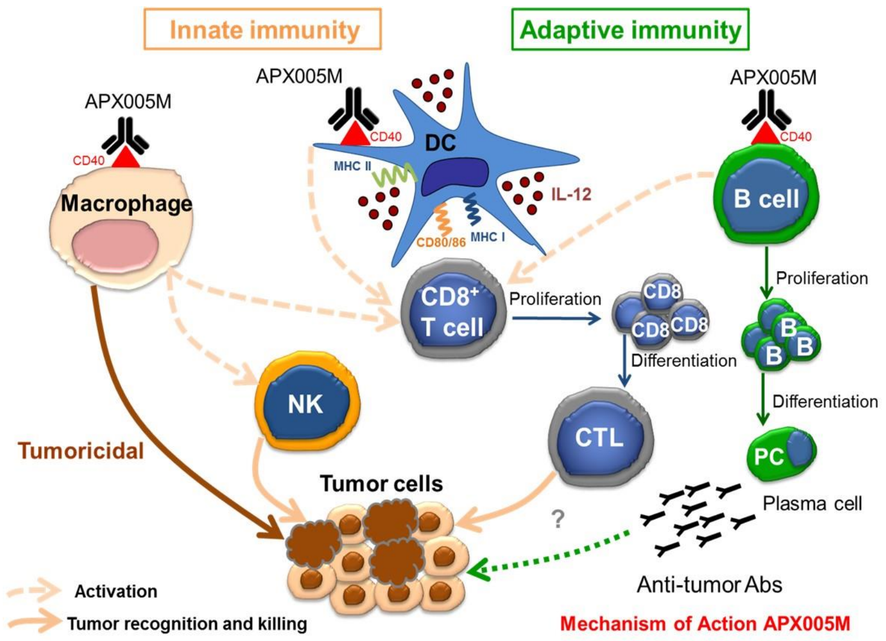
BACKGROUND



- APX005M is a humanized IgG1 CD40 agonistic antibody that binds with high affinity to human CD40 expressed on APCs

STUDY OBJECTIVES

- Assess the safety and tolerability.
- Define the maximum tolerated dose (MTD) and/or recommended phase 2 dose (RP2D).
- Assess objective response rate (ORR) at 12 weeks based on RECIST 1.1 at RP2D.
- Measure biomarkers in blood and tumor.

TRIAL DESIGN

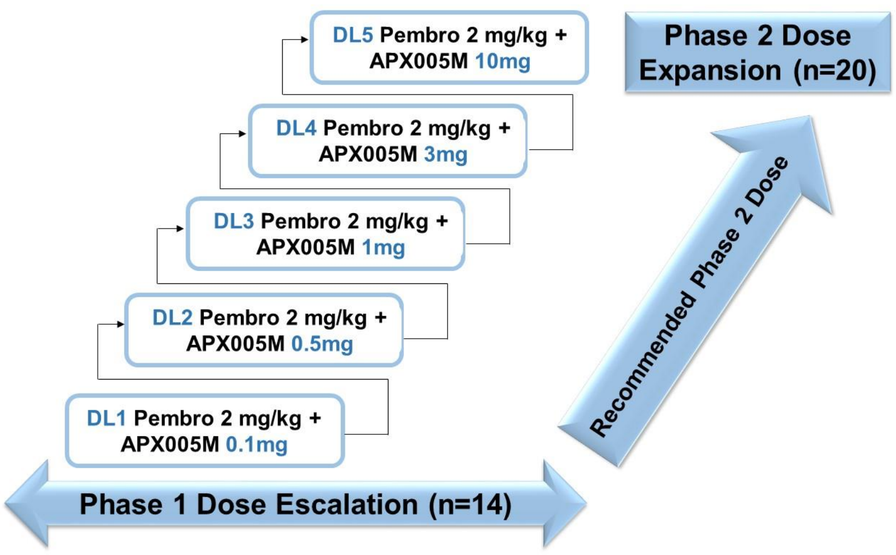


Table 1. Patient Characteristics

Characteristic	Total n (%) (N=14)
Age – median yr (range)	73 (48-81)
Sex, n (%)	
Male	11 (78%)
Female	3 (22%)
ECOG performance status n (%)	
0	10 (71%)
1	4 (29%)
2	0 (0%)
Stage n (%)	
III	5 (36%)
IV M1a or M1b	4 (28%)
IV M1c	5 (36%)
Lactate dehydrogenase, n (%)	
≤ ULN	10 (71%)
≥ ULN	4 (29%)
BRAF V600 Mutation, n (%)	
Positive	6 (43%)
Negative	8 (57%)
PD-L1*, n (%)	
Positive	4 (29%)
Negative	6 (42%)
Unknown	4 (29%)

*PD-L1 positivity with immunohistochemistry defined by ≥ 5% of tumor cells

Safety

- The combination of APX005M with pembrolizumab did not induce dose limiting toxicity at any dose level of APX005M.
- No study discontinuation due to TRAEs.
- No G3/4 immune-mediated AES.
- No immunosuppressive therapy needed.
- Most treatment-related adverse events were injection-site reactions.

RESULTS

Table 2.
Best Overall Tumor Response by

	Total n (%) (N=14)
Total Evaluable	14
Complete response	1 (7%)
Partial response	6 (43%)
Stable response	2 (14%)
Progressive disease	5 (36%)

Data cutoff 02 May 2019

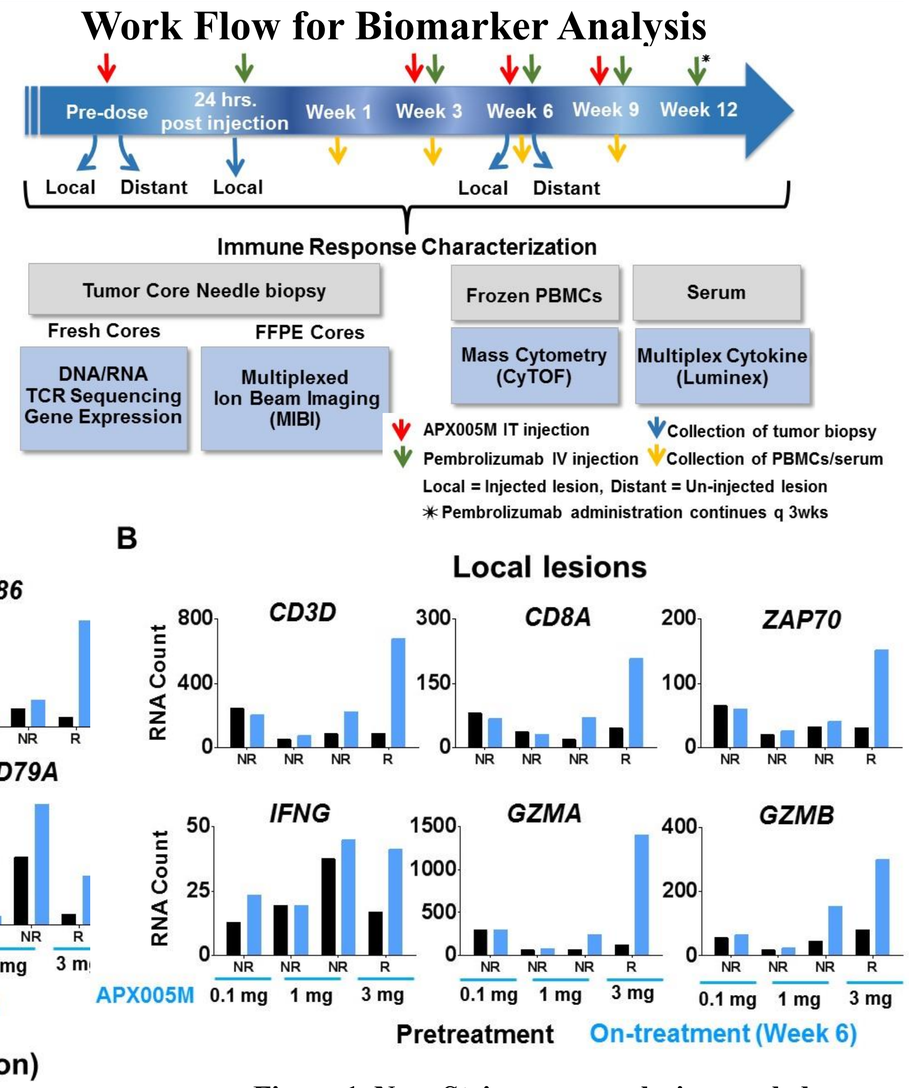


Figure 1. NanoString gene analysis revealed an induction of broad innate and adaptive immune activation in the responding patient. NanoString gene analysis to quantify transcript levels was performed on 4 matched baseline and on-treatment tumor biopsies. (A, B) Selected genes related to co-stimulation/antigen presenting cells and cytotoxic/effector functions on local lesions (C) Selected genes related to co-stimulation/antigen presenting cells and cytotoxic/effector functions on distal lesion in the responding patient.

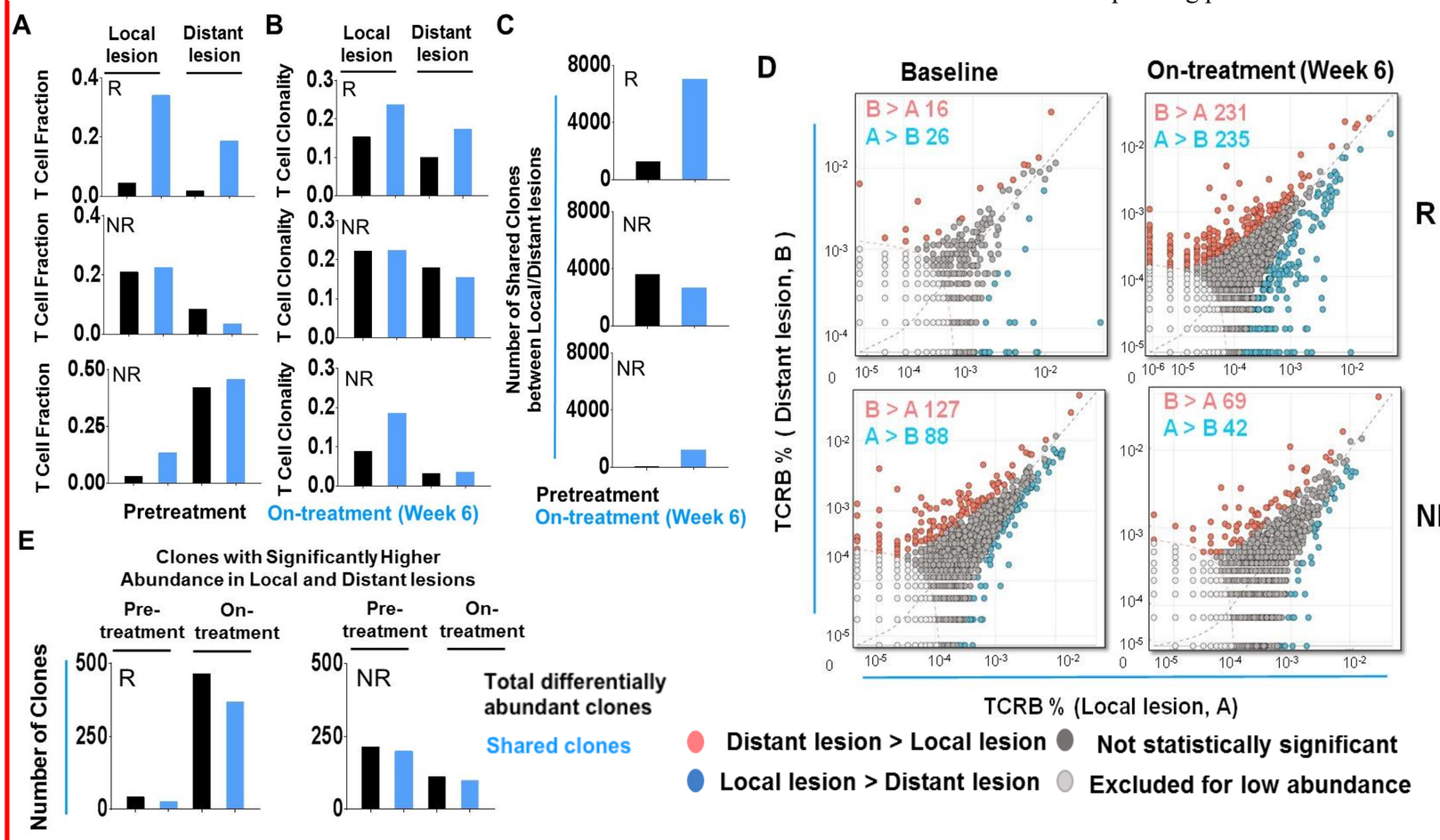


Figure 2. TCR sequencing analysis demonstrated an increase in T cell infiltration and clonality post treatment only in the responding patient reflecting the induction of a more oligoclonal T cell repertoire (A) T cell fraction (B) T cell clonality (C) Number of shared clones between local and Distant lesions at baseline and on-treatment (D) Scatter plot of T cell clones frequencies (from tumor biopsies collected before and after treatment in local and distant lesions) with differentially abundant clones annotated in red or blue as determined by binominal model (E) Number of clones with significantly higher abundance between local and distant lesions, total differentially abundant clones (Black) and shared clones (Blue)

CONCLUSION

- APX005M in combination with Pembrolizumab is well tolerated.
- APX005M in combination with Pembrolizumab showed encouraging anti-tumor activity.
- Preliminary biomarker analysis demonstrates that combination of Pembrolizumab with APX005M can induce broad innate and adaptive immune activation in both local and distant lesions.

ACKNOWLEDGMENTS

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