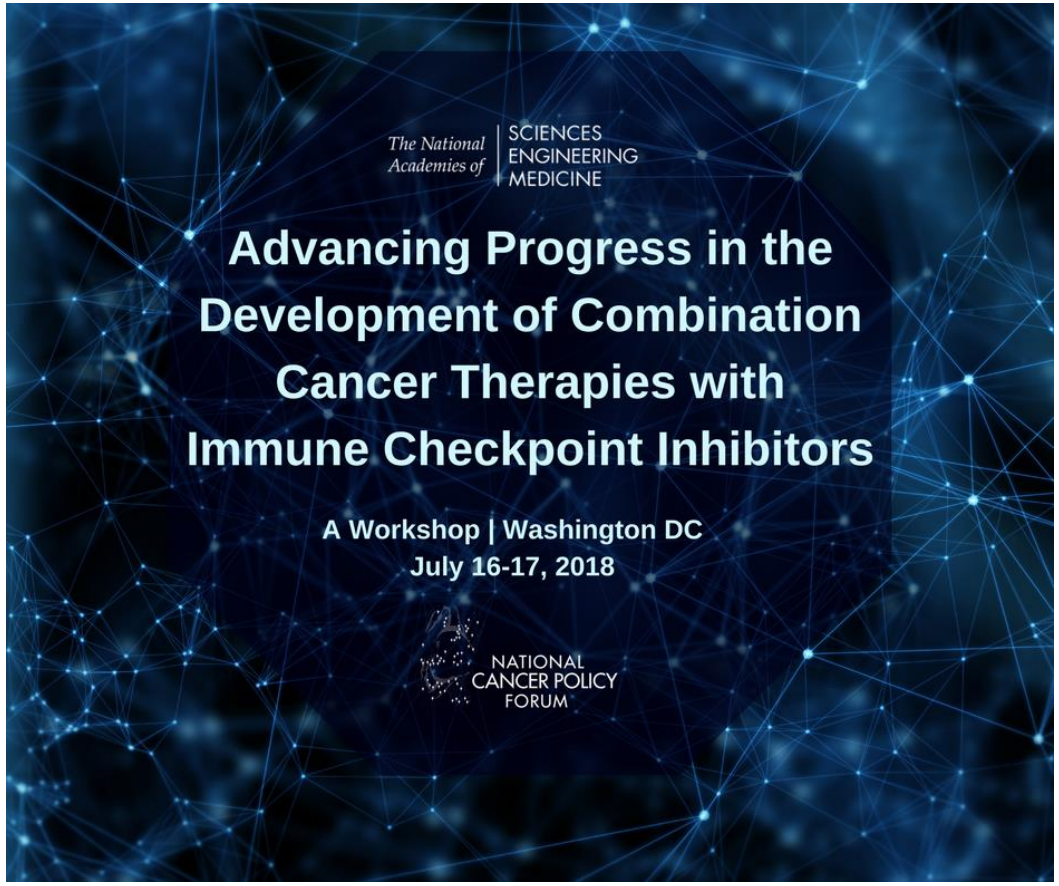
The National Academies of | SCIENCES ENGINEERING MEDICINE

WORKSHOP WRAP UP



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Co-Chair, Workshop Planning Committee

Session 1: Overview of PD-1/L1 Therapy and the Need for Combination Therapies

- The landscape is crowded with many IO molecules in development and many trials in progress "spaghetti model"
- PD-1/PD-L1 inhibitor combinations in lung cancer are transforming the treatment landscape
- Not for profit organizations and preclinical approaches have a role to play
- Phase 1 trials can be improved to detect clinical signals
- Immunotherapy combinations may operate by independent treatment effects as opposed to additive or synergistic effects

Session 2: Overview of Biomarker Development for Immune PD-1/L1 Checkpoint Blockade Combinations

- Immunohistochemistry – the status quo – likely to require additional information to increase sensitivity and specificity
- Genomic testing (targeted and TMB) – promising but needs standardization (under way).
- Expression (mRNA) signatures – promising, needs more evidence, maybe in single cells someday
- The microbiome, promising, or not… Computational concerns: reproducible, but not statistically significant when adjusted for multiple testing

Session 3: Clinical Trial Design for PD-1/PD-L1 Combination Therapies

- Correlative science, including but not limited to what is traditionally considered a “biomarker”, can enhance our understanding of mechanisms of action and so inform combination trial design.
- Quality biospecimens collected, stored and shipped using robust protocols, as well as validated assays, are needed if correlative science and biomarkers are to be reliable and valuable
- Patient (customer) perspectives need to be integrated into the design of trials if they are to have optimal impact on interpretation of results

Session 4: Regulatory Challenges with Developing PD-1/PD-L1 Combination Therapies

- Enlightened FDA willing to provide incentives (e.g., no user fees) to expand labels for combos
- Regulatory guidance clear regarding contribution of components and cross labeling of drugs
- A truly collaborative environment between regulators and companies to get these combos to patients

Session 5: Precompetitive Data Sharing and Collaboration to Develop PD-1/PD-L1 Combinations

- Real world data offer the opportunity to observe the interrelationship between diagnosis, treatment, and outcomes at scale
- To achieve this we must solve the challenges of data aggregation, curation, and confident assessment of data quality
- Integrating biomarkers with real world data to improve patient selection
- Use digital basis of INFORMED architecture to speed safety reporting and accelerate FDA review for drug approval