27th Annual Cancer Progress Day 2 Recap

Cancer Progress by Defined Health
New York, NY | March 8-9, 2016

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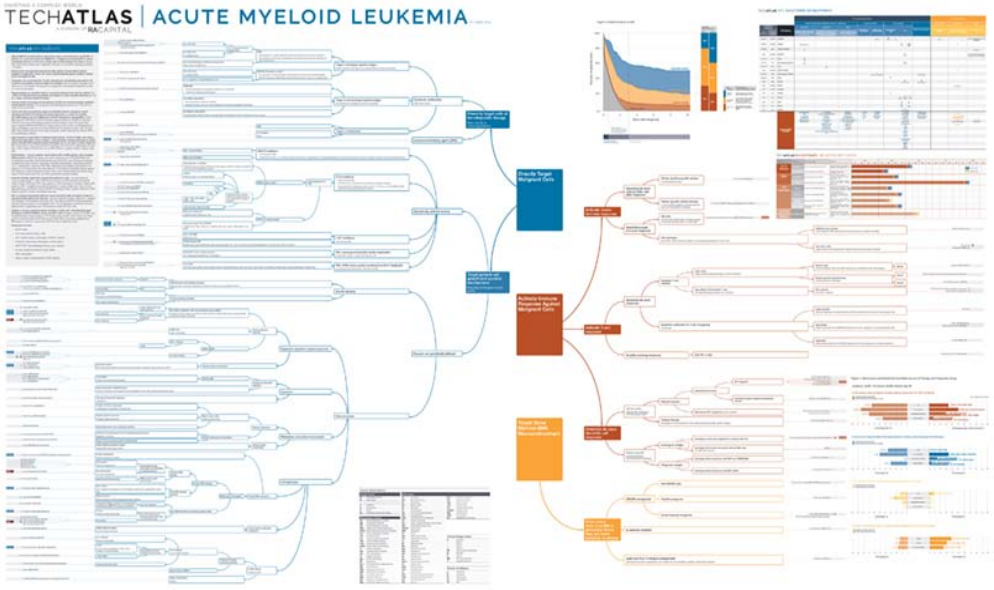
THERAPEUTIC INSIGHT by Defined Health

CANCER PROGRESS by Defined Health

Cancer Progress 27: Day 2 Recap

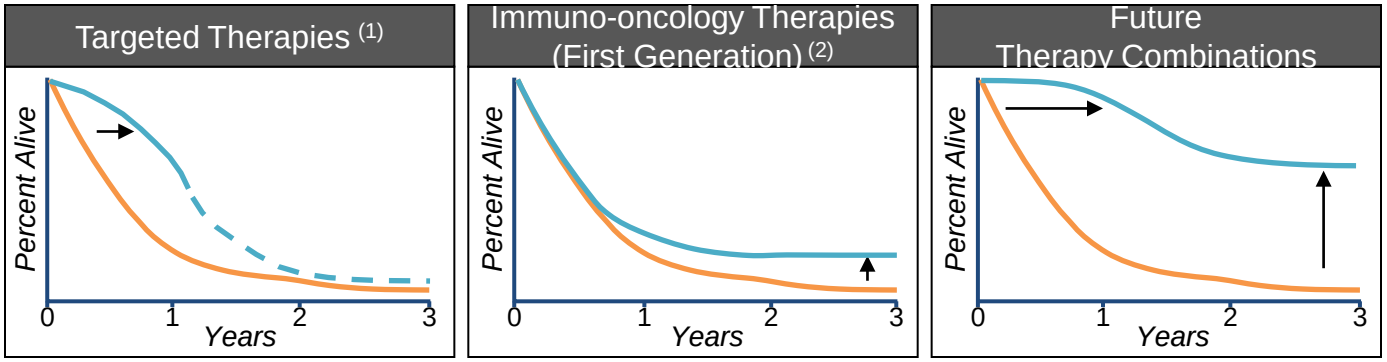
- **8:15 – 9:15am Keynote: The Game Theory of the Global Cancer Moonshot**
  Peter Kolchinsky
  - TechAtlas maps to determine a coordinated strategy among different indications - “Chess pieces” of industry
  - Solutions matrix visualizes which assets each company has to assemble a toolkit
  - Matrices are highly predictive of which moves will be made because some moves will be inevitable
  - Collaboration with investigators to use maps to create and design a melanoma moonshot program (MICAT)
  - A potential ‘Trojan horse’ for players who are behind in the IO space to push forward (control of multiple assets)
  - Smaller companies should care more about their agents’ role in a combination than as a single agent
  - Importance of safety in combos



RA Capital website

Cancer Progress 27: Day 2 Recap

- **9:15 - 10:30am Immuno-Oncology I: Attacking Cancer Antigens- Exploiting off-the-shelf and Personalized Vaccines and Triggering of Immunogenic Cell Death** *Jeffrey M. Bockman, Defined Health*
  - How to treat “cold tumors” (getting T-cells to infiltrate Class I negative tumors)
  - Must find the right pathways to modulate – vaccines have a role in modifying the microenvironment.
  - Multi-antigen approach to overcome antigen escape
  - Stimulate an antigen cascade effect that results in neoepitopes being expressed and targeted by the immune system.
  - Preclinical models most useful for elucidating MOA; less so for predicting efficacy in humans.



Andrea van Elsas

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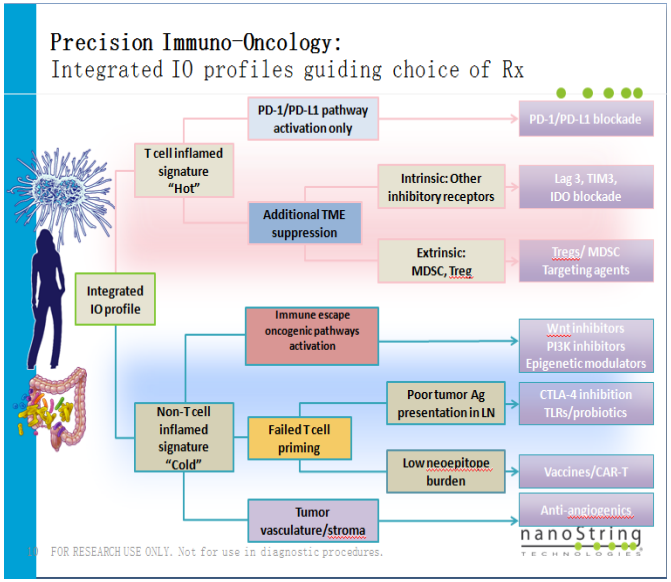
- **10:45am – 12:00pm: Immuno-Oncology II: Next Wave IO Targets and Modalities**
  Jeffrey M. Bockman, Defined Health
  - Incredible increase in combination IO trials between 2014 and 2015 primarily being sponsored by large Pharma.
  - Best to focus on T-cell inflamed (hot) tumors (commercial risk) v. non-inflamed (cold) tumors (technical risk)?
  - Important for novel technologies to demonstrate complementarity to checkpoint inhibitors
  - Focus shifting from extracellular to intracellular targets with advent of novel technology/MOAs and improved understanding of biology
  - Infinitely large number of potential combinations, sequencing, patient selection; very difficult to predict how assets will be positioned
  - Structure combination trials in a more rational way
  - Transplantable tumor models are useful to explore the tumor microenvironments and inform prioritization for clinical development



Alessandra Cesano

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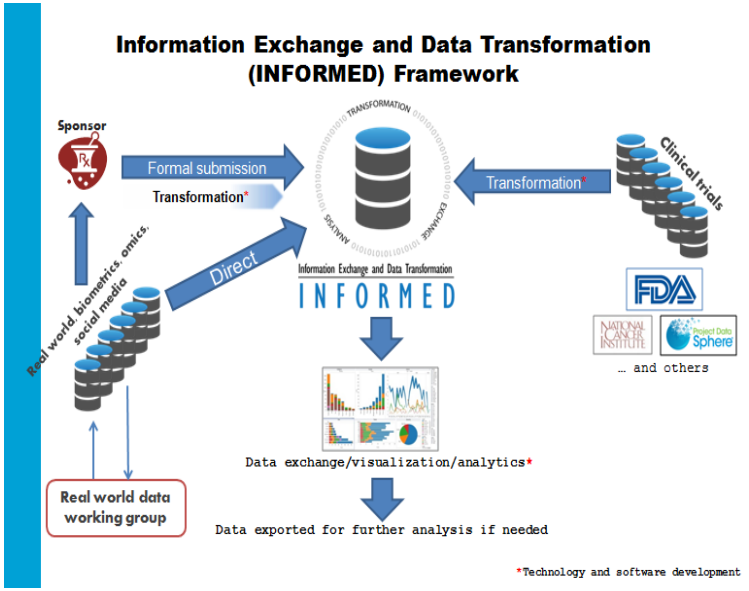
- **1:15 – 2:30pm N-of-One Trials: Is This the Future of Oncology Drug Development?** *Brian Leyland Jones, Avera Cancer Institute*
  - Patient-oriented trials: Get a better understanding of why someone may or may not respond to treatment.
  - Vetting algorithms for matching patients and drugs. No two patients will have the same neo-antigen “cocktail”
  - Assimilate all of the signaling pathways in the tumor to understand what drug combination ought to be best
  - The current paradigm faces the challenge of the need for more single arm trials for approval.
  - Fundamentally think of diagnostics differently within N of 1 trials.
  - Move towards building a multi dimensional model towards capturing tumor responses and kinetics.
  - INFORMED Network initiative



Sean Khozin

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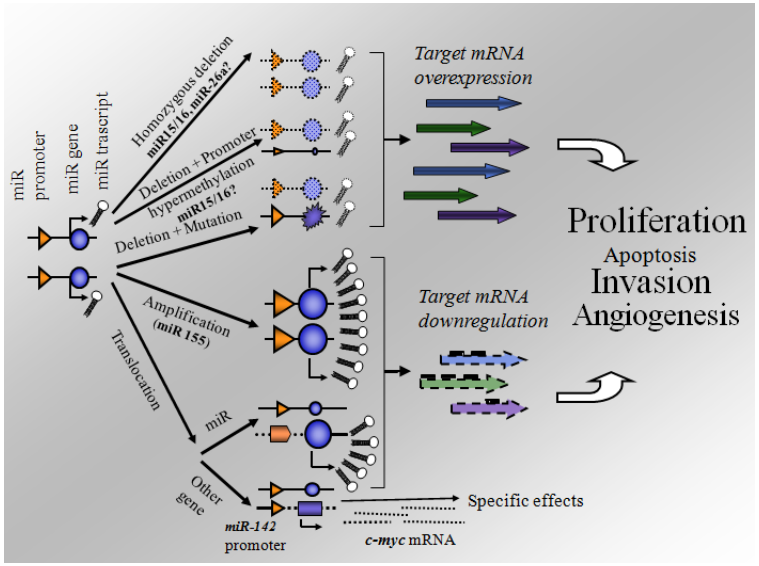
- **2:30 – 3:45 Novel MOA: RNA as a Target and a Therapeutic**
  Mike Rice, Defined Health
  - A number of RNA programs are in preclinical and clinical development. A potential $6B market by 2020
  - MiRNA can be used as a diagnostic, prognostic, monitoring, and therapeutic. MiRNA can inhibit multiple oncogenic pathways
  - mRNA can induce synthesis of transmembrane proteins. Many proteins can be made from one RNA – easy to enable combinations
  - Cost differential between testing oncology targets in mice v. in humans (2000x more expensive)
  - Not going to be one size fits all for selection of nucleic acid or delivery vehicle.
  - Intratumoral delivery lends itself to immunotherapy. Only need to transfect a small percentage of cells to experience abscopal effects.



Carlo Croce