26th Annual Cancer Progress Day 2 Opening Remarks

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Cancer Progress 26: Day 1 Recap

- **8:15 – 9:15am Plenary Keynote: Progress, at What Price? (moderated by Ed Saltzman)**
  - Prescription products have increased 15%/year. Unsustainable projected costs of novel combination regimens.
  - Broken market for drugs: bad for innovation, patients, & efficient economy
  - Disconnect between costs and value – Patients face financial toxicity
  - Health Technology Assessment
  - Comparative effectiveness – Value based pricing
  - Care delivery reform is separate from cost of drugs- needs to be approached differently
  - If payers treat (for example PD1) drugs as a class then companies will have to price competitively
  - 100 fold increase in price of new cancer drugs since 1965
  - Solution needs to be transparent and simple
  - Exclusionary Biomarkers or Identify right person for therapy and prove value

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- **9:15 – 10:30am A Day in the Life of a Breast Cancer Doctor: Integrating Omics to Optimize Patient Outcomes**
  - Personalized cancer management strategies based on genetics (multiple platforms)
  - Progressively moving to sequencing every patient upfront
  - Cancer is changing from disease of location to disease of driving genomic alterations
  - Changing role of pathologist: Repeat biopsies tracking evolving tumor
  - Therapeutic strategy to inhibit all escape pathways
  - Case study: Salvage of complicated advanced breast cancer with 5-6 TKI cocktail
    - Issues: Costs/reimbursement
  - Improvement in CLIA and FDA IVA needed
  - Clinical utility required by (most) payers for reimbursement for diagnostic test
    - Currently not required by LDT or IVD
  - Umbrella trials – 6 triplet combinations
  - Tissue sampling → Omics analysis → Bioinformatics → Treatment matching

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- **10:45 – 12:00pm Tumor Panel I: Rare and Pediatric Cancers**
  - 350K survivor of ped. cancers – many living with late effects of treatment
  - Currently Ped. drugs come from adults – Need a rational basis for initial development for childhood cancer due to different mutational drivers, child development, late effects.
  - COG (230 institutions) is well organized/uniform and enrollment is straight forward, although the cancers are rare
    - 60% clinical trial enrollment.
    - Issue is getting access to drug before Phase II.
  - Clinical development for cure, not relapse
  - Ped. Drug regulation ODAC/PREA/BPCA
  - Issues with clinical endpoints, often compared against historical control
    - Low patient populations (often <100)
    - Very young patients (< 6 years old)
  - Genomic sequencing, tissue banking.
  - Target initiation: Genomic studies for five high risk cancers
  - Large biopharma, child centric development programs to ensure access.
  - Matrix trials

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- **1:15 – 2:30pm Immunotherapy I: Targeting Checkpoint, Co-Stimulatory and Novel Immunomodulatory MOAs**
  - "The combination is the drug" – need to be proven clinically
  - PD1 appears well-tolerated as a "backbone" starting point for combinations
  - Mouse models may be helpful for combos, not for drug sequencing
  - Preclinical mechanistic science will bring forth combination possibilities that need to be tested in clinic
    - Finite collection of possible immunotherapy combinations
  - End of "one size fits all" approach for combination therapies
    - Pharmacological window may differ between patient populations. More fine-tuning than monotherapy
  - Need for antigenic stimulation – SOC (e.g., TKIs), vaccines, oncolytic virus
  - Differentiating multiple similar agents (PD1s)
  - Targets other than T-cells
  - Tumor microenvironment holds many new cells and targets – TAM, CAF
  - Biomarkers – TIL infiltration, PD-L1 levels, others?
  - Neoantigens- May predict responsiveness.

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- **2:30 – 3:45pm Immunotherapy II: Engineered Cell Therapy**
  - Update on the state of the current status of CAR T-Cells and TCRs
  - More mature CAR19 T-Cell data shows 70-90% durable CR in ALL, but lower responses in other B-Cell malignancies
  - T-cell therapy must have consistent safety and efficacy profile from patient to patient
  - Incorporating features to improve efficacy on bulky tissues and microenvironment
  - What is the “right amount” of disease to target? – Is there too much tumor to treat with CAR T-cells?
  - Addressing: safety CRS and potential off tumor toxicities
  - Additional targets antigens, broader tumor types
  - Safety switches and controlling proliferation
  - Novartis is working on advancing T-Cell technology and standardized , saleable manufacturing

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- **4:00 – 5:15pm Tumor Panel II: B-Cell Malignancies: Recent Advances, Remaining Challenges and Promising New Approaches**
  - Provide an overview of recent advances in CLL (and NHLs).
  - Recently approved agents (glycoengineered CD20 mAb, BTK, PI3Kd)
  - What's in development (next in class agents, Bcl2, antibodies, immunotherapies)
  - How are they likely to impact treatment algorithms in the future? How to sequence and combine? Intermittent vs. chronic therapy?
  - Remaining challenges/issues: tolerability, resistance, Richter's transformation
    - MRD relationship with outcomes, how to gain absence MRD
  - Abbvie's focus on B-Cells around Venetoclax and BCR pathway inhibitors.
  - Combinations regimens that improve efficacy while minimizing the toxicities.
  - Address costs of novel combination regimens and value to patient.

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- **5:15 – 6:30pm Combination Therapies: Challenges and Opportunities**
  - How to study, rationale, industrialized v. empirical
  - Challenges and Opportunities:
    - Predictive models
    - Optimal combos: Start early stage or later in disease
    - Dosing & Scheduling : Appropriate schedule among multiple drugs.
    - Efficacy: What type of endpoint to use. How to establish there is a signal
    - Safety and Tolerability: Resistance and tumor heterogeneity
    - Patient Population: Tailoring combinations
    - Cost: Partner drugs between different companies/ Pricing models
  - Many therapies (ex. vaccines) that haven't worked as monotherapy can be useful in combos
  - Synthetic lethality
  - Commercial slant of franchise expanding and challenges of internal-external partnerships
  - Determining the incremental value (TPP) to make go/no go decisions
  - Value/pricing for combination

Technology and Big Data: Transforming Cancer Research and Care

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