30th Annual Cancer Progress Conference

Discussion Points on Immuno-Prevention

CANCER PROGRESS
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Nicholas J. Sarlis, MD, PhD
Chief Medical Officer
SELLAS Life Sciences Group, Inc. – New York, NY

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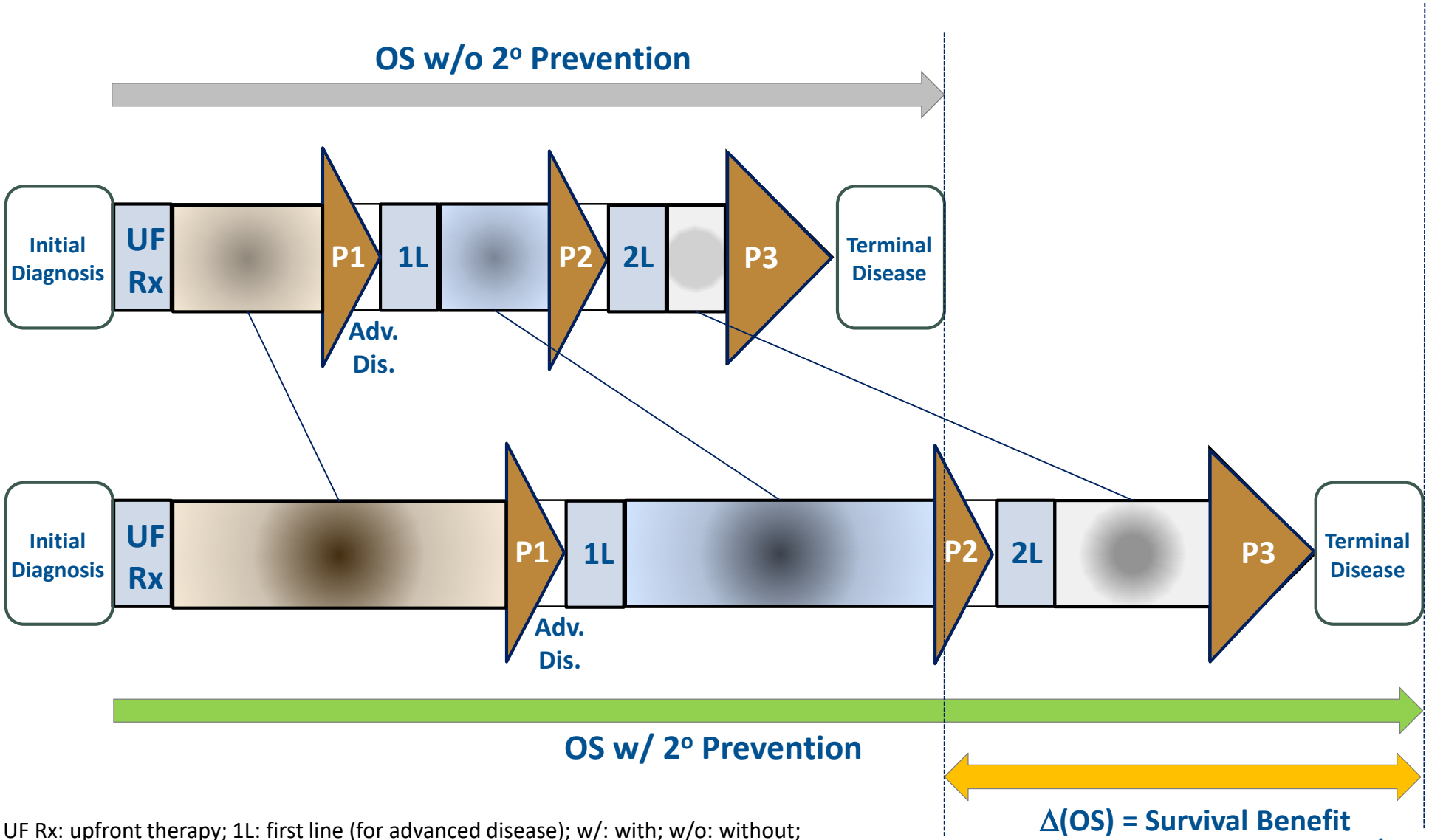
- *Dr. Sarlis is an Officer of SELLAS and holds equity in the company.*
- *He also holds shares of Sanofi and Incyte Corp.*

SECONDARY PREVENTION IN CANCER

- Implementation of therapeutic modalities in the **maintenance/ consolidation** or **adjuvant setting** to **prevent or delay** the recurrence/relapse of disease after successful prior debulking
    - This could be in the context of local/regional and/or distantly metastatic disease; however, it is typically for the latter
    - Monotherapy vs. combination Rx
    - Can be implemented after 1st, 2nd, 3rd, …nth line of therapy (depending on the tumor type and degree of unmet medical need)
    - Potential for prolonged periods of administration (if effective)

- Ideally should be associated with:
    - **low/manageable toxicity burden** and
    - **lack of appreciable tumor 'escape'** from its therapeutic effect

Prolongation of Progression-Free Interval (PFI) should lead to improved Overall Survival (OS)



UF Rx: upfront therapy; 1L: first line (for advanced disease); w/: with; w/o: without;
2L: second line; P1,2,3: progression episodes 1,2,3; Adv. Dis.: advanced disease

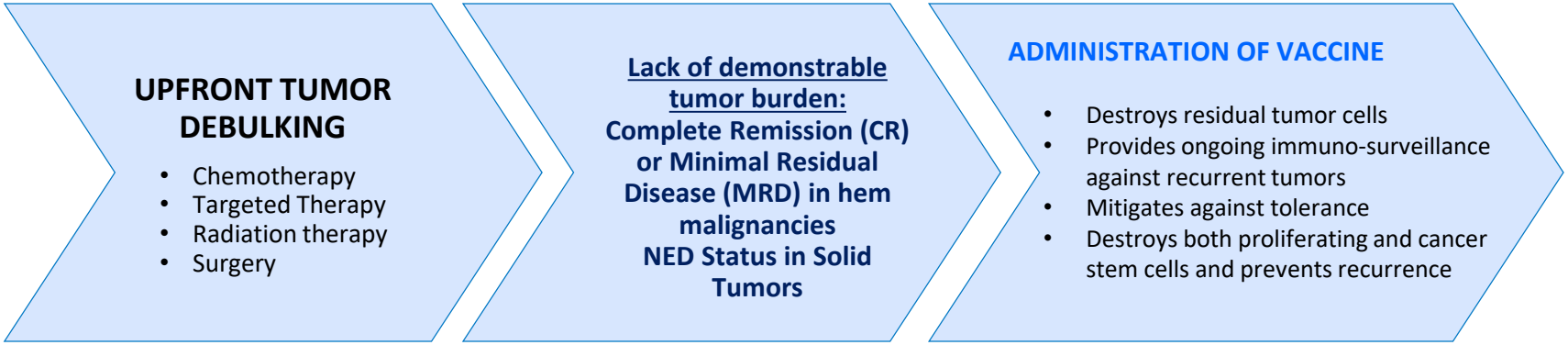
SECONDARY PREVENTION IN CANCER

Types of Agents Used:

- Chemotherapy
  - numerous regimens in lymphomas, Stage 3 NSCLC/CRC, etc.
- Radiobiologics
  - 131-I (radioiodine) in thyroid Ca
- Targeted biotherapy
  - VEGF inhibitors in mesothelioma; PARP inhibitors in ovarian Ca; EGFR inhibitors (SCCHN); Endocrine therapy (Prostate/BrCa); assorted TKIs, etc.
  - Novel pathways: Tumor metabolic reprogramming (OxPhos inh); microbiome alteration, etc.
- Immuno-Oncology (IO) Agents & Tumor Microenvironment (TME) Modulators
  - Interferon & Cytokines (renal Ca, melanoma)
  - Stem Cell Transplant (autologous in myeloma, allogeneic in AML, etc.)
  - Immune synapse modulators (Checkpoint blockade, etc. in melanoma and other tumor types) and other IO agents (e.g., bispecific antibodies, TILs, CAR T-cells, etc.)
  - Peritumoral inflammation modulators (JAK inh, IDO/TDO inh, etc.)
  - **Cancer therapeutic vaccines**

PARADIGMS OF USAGE OF CANCER VACCINES

- AS MONOTHERAPY IN THE MAINTENANCE/ADJUVANT SETTING



- IN COMBINATION WITH OTHER THERAPIES (MAINLY IMMUNOTHERAPIES) TO TREAT MEASURABLE/ MACROSCOPIC ADVANCED DISEASE
  - Clinical trials studying the effect of the combination of cancer vaccines plus immuno-oncology (IO) agents vs. IO agents alone
  - Strong preclinical/ immunobiological rationale (in most cases)

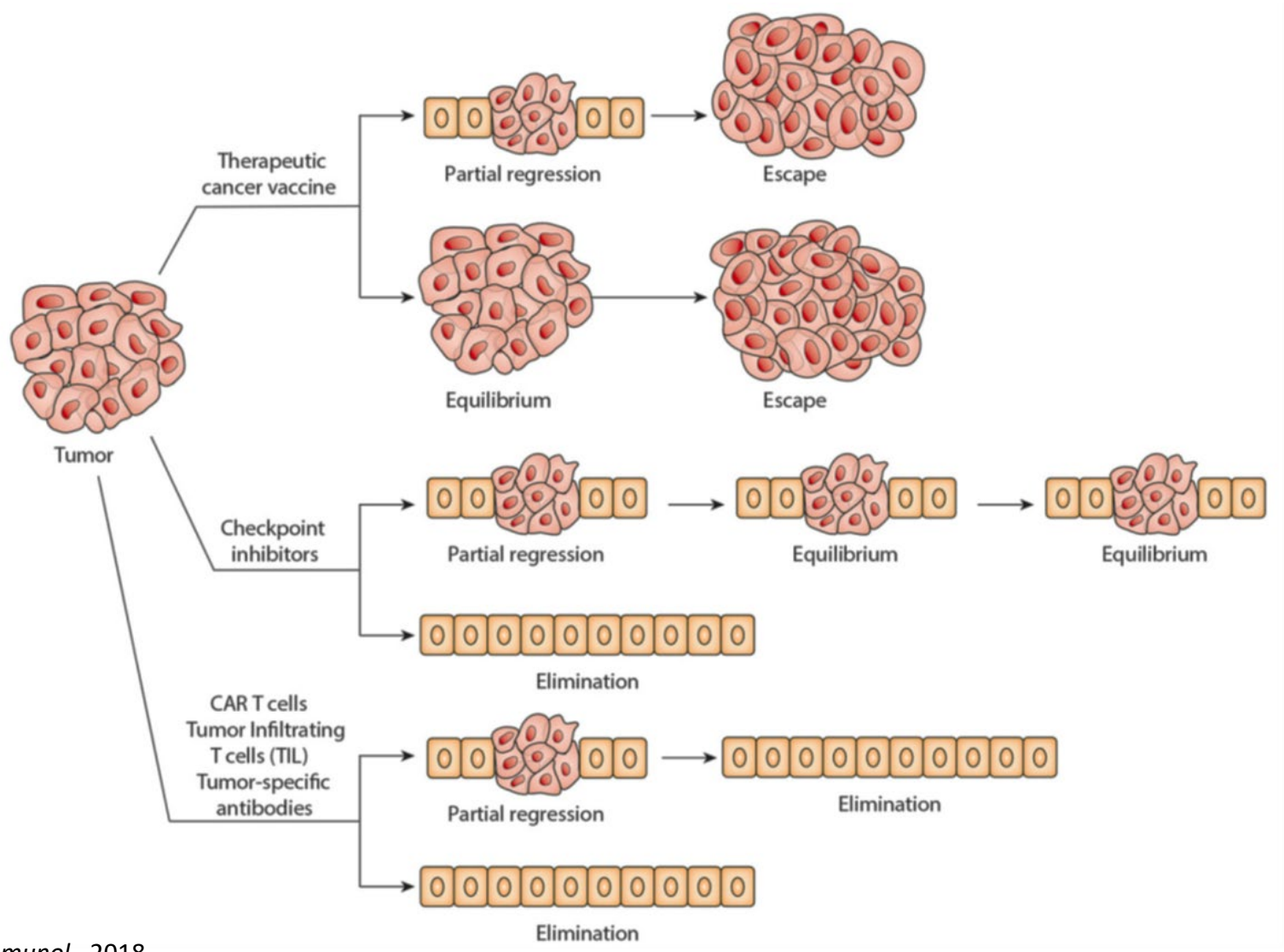
TYPES OF CANCER VACCINES

- Antigen vaccines
  - Protein/ Peptide vaccines
  - Vaccines against other types of molecules (e.g., glycolipids)
- Whole cell vaccines
  - Autologous
  - Allogeneic
- Dendritic cell (DC) vaccines
  - incl. ex vivo modified DC vaccines
- DNA vaccines
- Anti-idiotypic vaccines

PEPTIDE VACCINES – CHALLENGES & OPPORTUNITIES

- Ability to 'address' a large variety of antigenic targets (incl. intranuclear proteins)
- Valency/ "Spectrum"
  - "Wide-spectrum" vaccines (multivalent):
    - E.g.: Galinpepimut-S (anti-WT1) – tetravalent → wide variety of tumor types express the target antigen
  - "Narrow-spectrum" vaccines:
    - E.g.: Nelipepimut-S (anti-HER2) – monovalent, E39/J69 (anti-Folate binding protein) - bivalent
- Heteroclitic technology
  - By design mutated residues (cross-reactive with native fragment)
    - Improved antigenicity/ immunogenicity
    - Decreased tolerance
- "Off-the-shelf", relatively low manufacturing costs; low toxicity burden (no 'off-target' effects)
- Need for prestimulation with immune adjuvant (GM-CSF)
- Ideally, need to stimulate both CD8+ and CD4+ T-cells
- "Epitope spreading" is a highly desirable attribute and a biomarker of immunologically mediated cancer cell death
- Ideally, ability to be applied in a global scale (across HLA types; MHC Class I and II binding)
- Opportunity for inoculation boosters (~q.3-6 months) over long time periods

CANCER VACCINES: MECHANISM OF ACTION & EXPECTED OUTCOMES



Finn OJ. *J Immunol.*, 2018