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Final Results of a Phase II Prospective Trial Evaluating the Combination of Stereotactic Body Radiotherapy and Pembrolizumab in Metastatic NSCLC

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Disclosures

- Dr. Campbell works for the Yale University School of Medicine
- Dr. Campbell has no conflicts of interest to disclose

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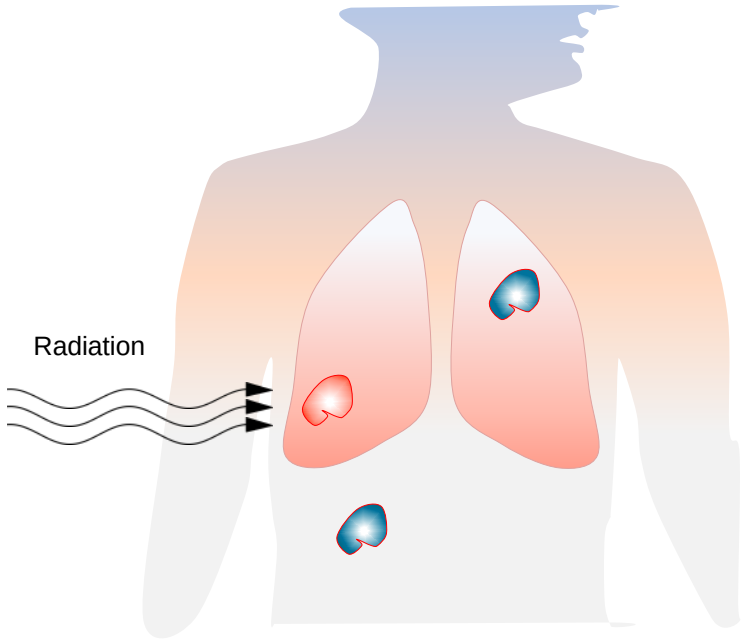
Background

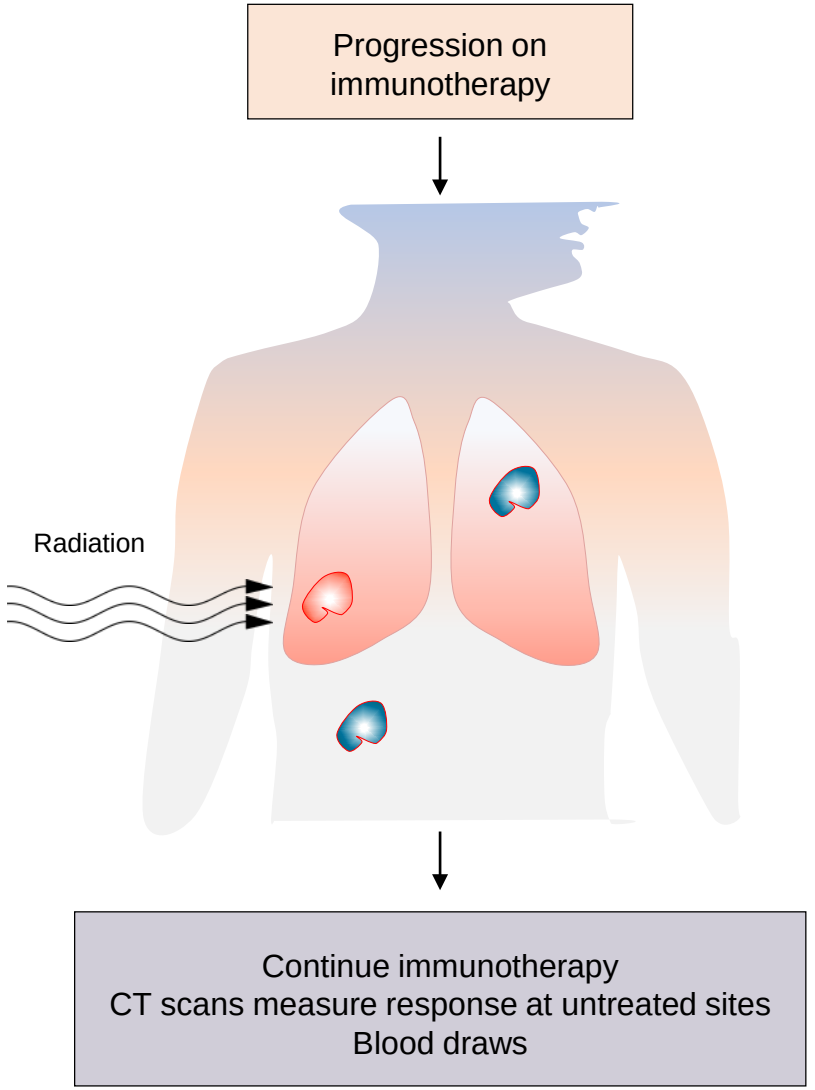
- **Why this trial:**
  - We need more therapies for patients with metastatic lung cancer
  - Immunotherapy activates the immune system to attack cancer
  - Adding radiation to immunotherapy has been shown to result in therapeutic synergy
    - When high dose radiation is given to patients on immunotherapy, tumors that weren't targeted by the radiation can shrink
    - This is called the "abscopal effect"

- **Trial Question:**
  - Can the addition of high dose radiation given in a few fractions to a single site of disease reinvigorate an immune response in patients who have progressed on anti-PD-1 therapy?



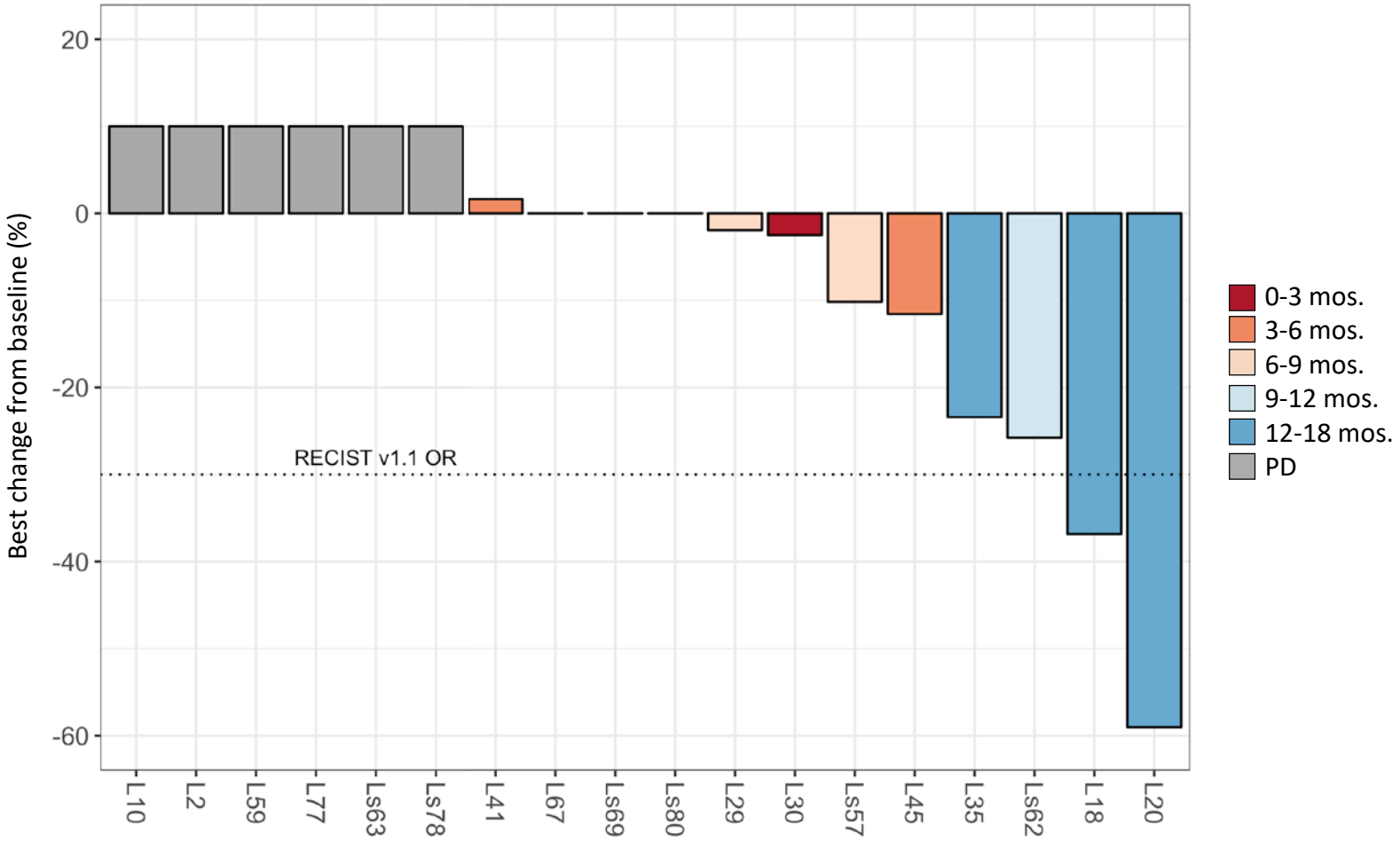
Trial Design

- **Patient eligibility**
  - Metastatic NSCLC
  - ≥ 2 measurable sites of disease (one for treatment, others for measurement)
  - PD-L1+ histology was NOT required
- **Methods**
  - After patients progressed on immunotherapy, we gave high dose radiation in 3 or 5 fractions
  - Only one site of disease was treated with radiation
  - Other sites of disease were measured and tracked over time
  - Blood was drawn so circulating immune cells could be characterized



Results: Responses occurred outside the radiation field

- Waterfall plot representing best change in OVERALL RECIST v1.1 score after SBRT
  - All patients had progressed on anti-PD-1 therapy at the time of SBRT
- Responses are abscopal and represent DISTANT DISEASE
  - The SBRT-target lesion is NOT reflected in this waterfall plot
- 3 patients achieved either a PR or SD that lasted for one year or more
  - Better responses trended toward lasting longer



Results: 10% of patients had a partial response that lasted > 1 year

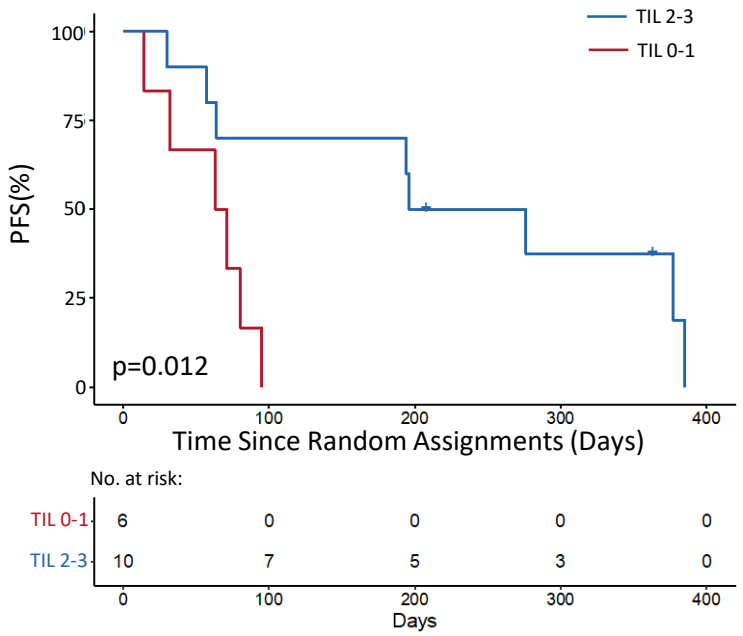
- Disease control rate: 57%
- 2 patients (10%) achieved a partial response sustained for longer than one year
- 10 patients (48%) achieved stable disease after SBRT
- PD-L1+ status trended toward increased PFS, but this did not achieve statistical significance

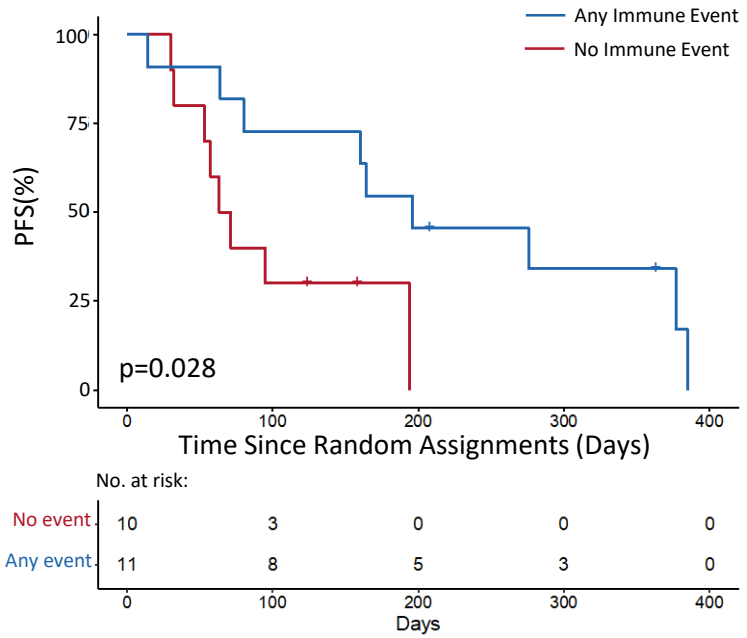
Outcome	
Median Overall Survival after SBRT	7.6 months (5.3-19.3)
Median Follow-up from time of enrollment (whole trial)	15.2 months (10.7-19.3)
Disease control rate after SBRT	57.14%
Patients achieving a PR after SBRT	9.52%
Patients achieving SD after SBRT	47.62%
Patients with PD after SBRT	28.57%
Patients with no scans after SBRT	14.29%
Median PFS after SBRT	4.1 months (2.1-6.5)
Median PFS after SBRT in patients with a PD-L1 status of 0	2.4 months (0.8-6.2)
Median PFS after SBRT in patients with a PD-L1 status > 0	6.5 months (2.1-12.1)
Median PFS after SBRT in patients with TIL scores of 0-1	2.2 months (0.8-2.9)
Median PFS after SBRT in patients with TIL scores of 2-3	6.7 months (2.1-12.1)
Median PFS after SBRT patients with NO immune-related adverse event	2.2 months (1.5-4.2)
Median PFS after SBRT patients with an immune-related adverse event	6.5 months (2.7-12.1)

Results: T cells in the tumor biopsy were associated with longer PFS

- Patients with TIL scores of 2-3 had a median of 6.7 months before disease progression; patients with TIL scores of 0-1 had a median PFS of 2.2 months

- Patients with ANY immune-related adverse event had a median of 6.5 months prior to disease progression; patients with NO immune-related adverse event had a median PFS of 2.2 months

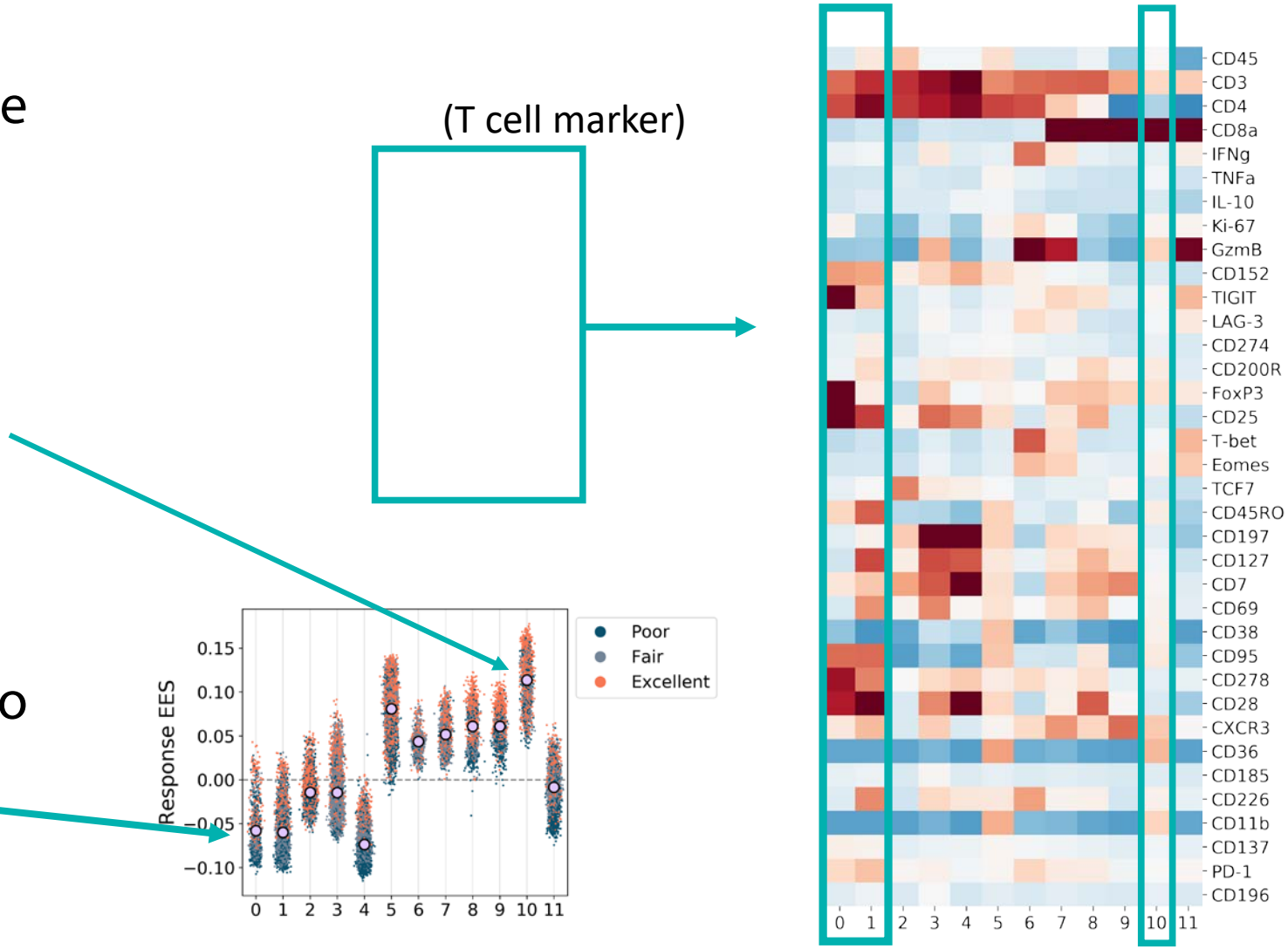




Outcome	
Median PFS after SBRT in patients with TIL scores of 0-1	2.2 months
Median PFS after SBRT in patients with TIL scores of 2-3	6.7 months
Median PFS after SBRT patients with NO immune-related adverse event	2.2 months
Median PFS after SBRT patients with an immune-related adverse event	6.5 months

Results: Patients who responded well had more CD8+ "killer" T cells in their blood

- CD8+ effector memory cells in the peripheral blood are enriched in patients with a partial response that lasted one year or more (cluster 10)
  - These cells can kill tumors
- CD4+ "regulatory" cells are enriched the peripheral blood in patients who responded poorly to SBRT (clusters 0 and 1)
  - These cells inhibit immune responses



Conclusions

- 10% of patients had a partial response that lasted > 1 year
  - These patients had already progressed on immunotherapy when they got SBRT
  - These patients had many sites of disease, but only got radiation at a single site
- Some responses were abscopal (occurred outside the radiation field)
- T cells in the tumor biopsy were associated with longer progression free survival
- Patients with an immune-mediated adverse event had longer progression free survival
- Patients who responded well to SBRT had more CD8+ "killer" T cells in their blood
- Patients who responded poorly to SBRT had more CD4+ "regulatory" T cells in their blood