

IASLC



**2022 World Conference
on Lung Cancer**

AUGUST 6-9, 2022 | VIENNA, AUSTRIA



Updates on Radiation Therapy for Stage III NSCLC

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DISCLOSURES

Company	Relationship(s)
RefleXion Medical	Research Support



Radiotherapy for Stage III NSCLC in the Era of Immunotherapy

- Definitive RT
- Neoadjuvant/Adjuvant RT
- Toxicity with RT and IO

Highlighting talks from:
Yi-Long Wu, Motoko Tachihara, Wilfried Eberhardt,
Willemijn Theelen, Ken Harada, Alexander Louie,
Andrew Bang, Shankar Siva, Nasser Hanna

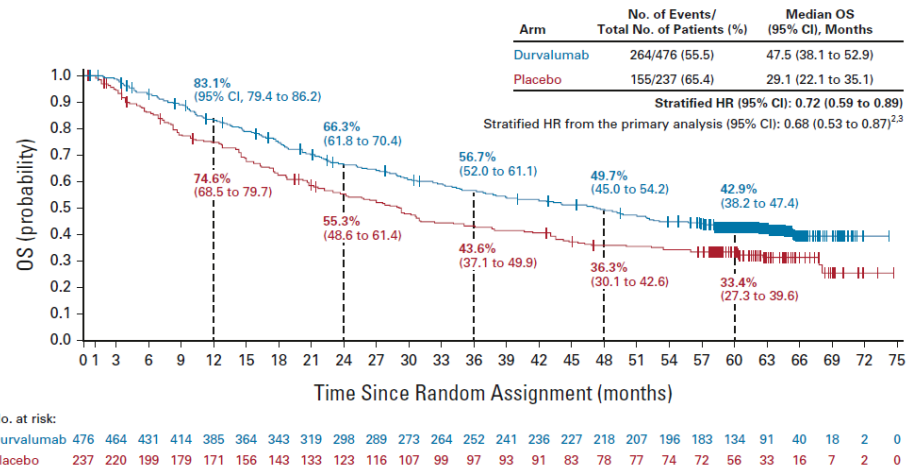




Radiotherapy for Stage III NSCLC in the Era of Immunotherapy : Definitive CRT

- Locally advanced disease effects ~30% of patients
- Adjuvant IO = new standard of care
- Unanswered Questions
 - Interactions between RT and IO
 - Multi-agent Adjuvant Therapy
 - Concurrent IO

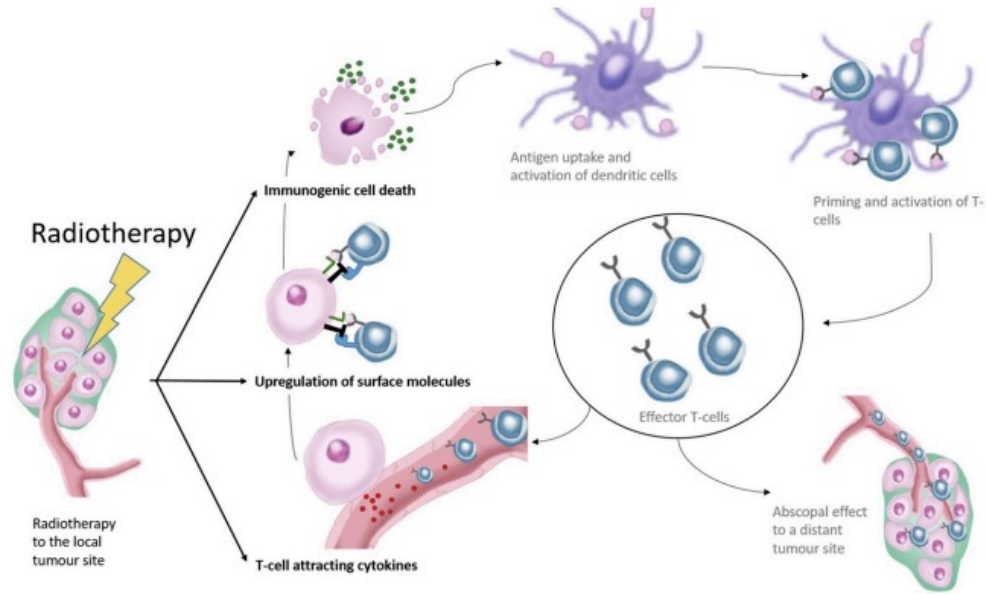
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Pacific Trial – 5-year survival data



Synergy between IO and RT

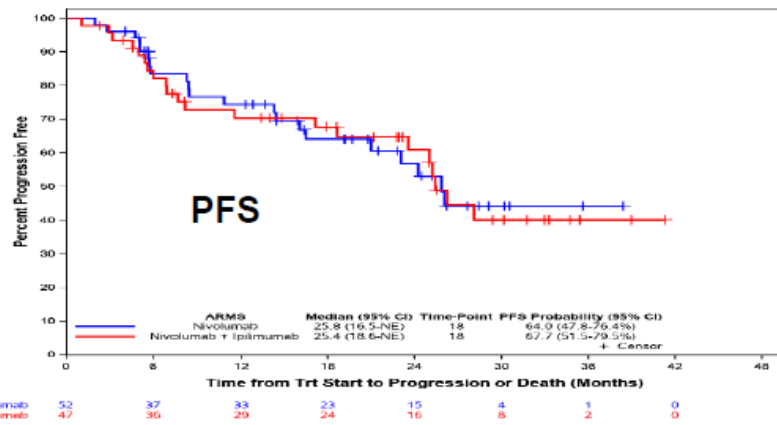




DEFINITIVE CRT: Multi agent adjuvant therapy?

Phase II Trial Hanna et al.:

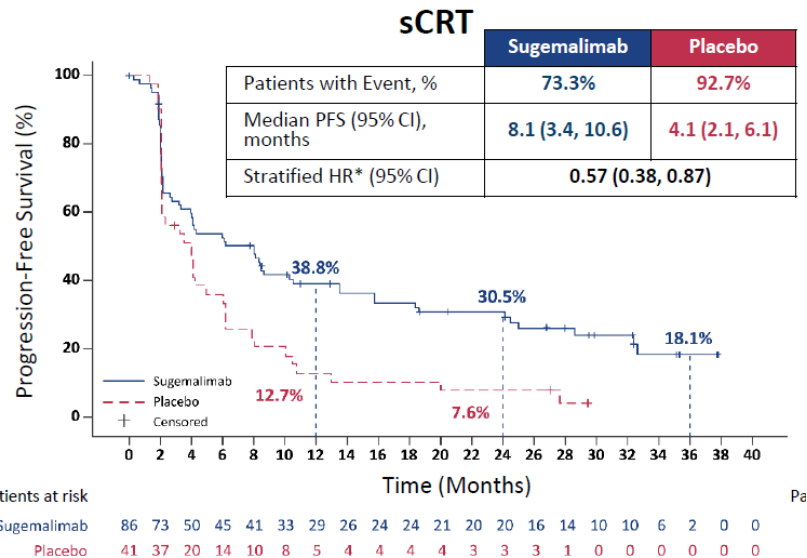
- Stage III CRT → 6 months adj nivo vs. 6 months nivo/ipi
 - Multicenter n=105
 - No difference in OS or PFS
 - Higher grade 2+ (22% vs 31%) and 3+ (9% vs 18%) w/ nivo/ip
 - 2 yr OS ~80% compares favorably to Pacific
- COAST Phase II Trial
 - Adj Durva (PDL-1) vs. D + Oleclumab (CD72) vs. D+ Monalizumab (NKG2a)
 - Combined therapy improved ORR and PFS over D alone





DEFINITIVE CRT: Benefit of Adjuvant IO w/ sequential Chemo → RT?

- GEMSTONE 301 Trial :
 - Stage III CRT → adj placebo vs. Sugemalimab (PD-L1 IgG4 Ab)
 - Patients treated with concurrent or sequential CRT
 - N = 381
 - 2 yr OS for sCRT: 71 vs 54% favoring Sugemalimab



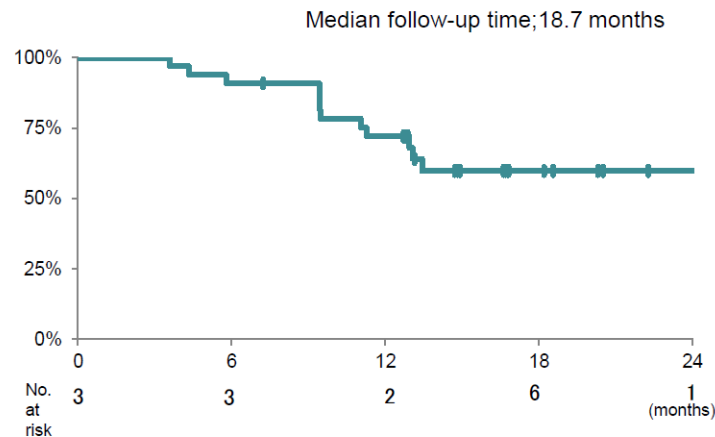


DEFINITIVE RT: Concurrent IO

- DOLPHIN Phase II Trial :
 - Stage III NSCLC, PD-1 $\geq 1\%$
 - N=35
 - RT w/ Concurrent Durva \rightarrow Adj Durva
 - Expected 12 month PFS of 50%
 - Grade 3+ pneumonitis 12%

- Phase III RCT – PACIFIC II

12-month PFS rate by ICR



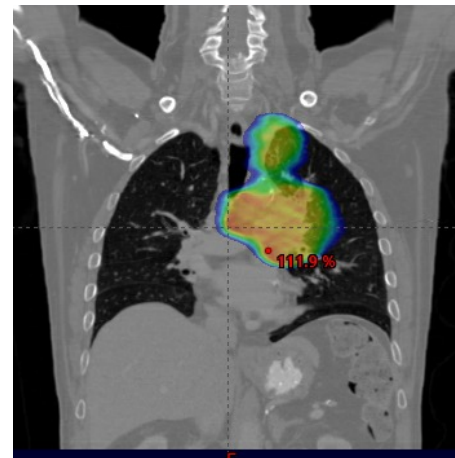
12-month PFS rate	90%CI (%)	95%CI(%)
72.1%	59.1-85.1	56.1-87.6





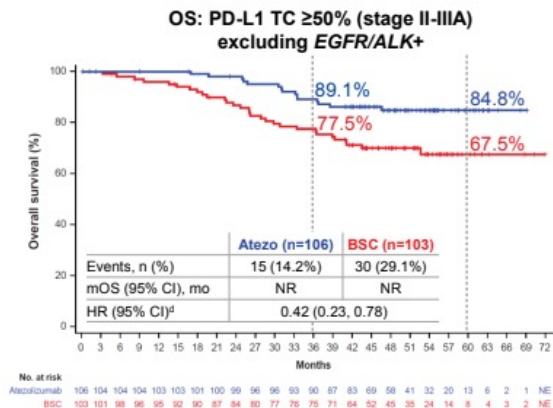
Definitive CRT: How to Optimize RT?

- Technologic Advances
 - IMRT, Respiratory Management, Protons
 - PET Guided Radiation
- Immune structures as OARs?
 - ICIs need T cells to work, Priming of T cells in lymph nodes





RT in Era of Immunotherapy: Role for RT in Resectable Stage III Patients?

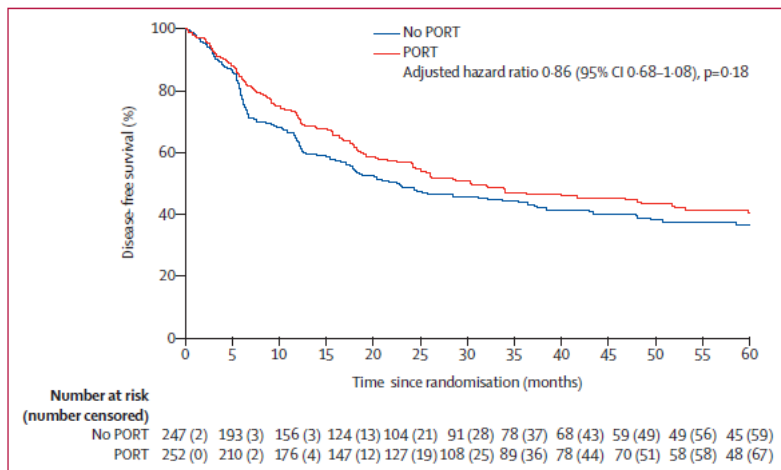


- Adjuvant RT?
- Neoadjuvant RT?

Impower 010, Felip et al. WCLC 2022



Resectable Stage III: Adjuvant RT?



- **LUNG ART**
 - Adjuvant RT for pN2
 - No difference in OS at 3 years (69 vs 67%)
 - Mediastinal relapse better in PORT arm, (46 vs 25%)
- Many Still Recommend RT for ECE, bulky, multi-station
- PD-L1 Status?
- Timing w/ systemic therapy?



Resectable Stage III: Neoadjuvant RT?

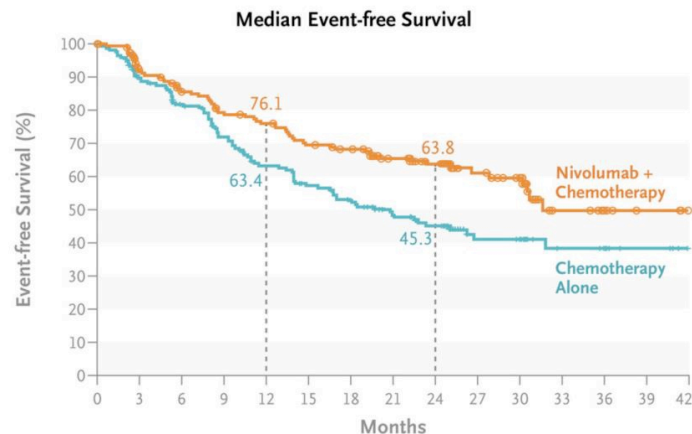
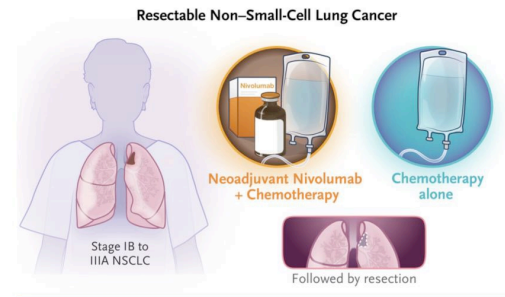
Checkmate 816 Stage IB-III A

- Pathological complete response (pCR) rate of 24.0% versus 2.2% with chemotherapy alone
- Major pathological response (MPR) rates of 36.9% versus 8.9%
- 16.7% of patients in nivo+chemo arm did not undergo surgery

Future Directions:

- Combining Neoadjuvant RT and IO?

1. Siva WCLC 2022 2. Forde NEJM 2022



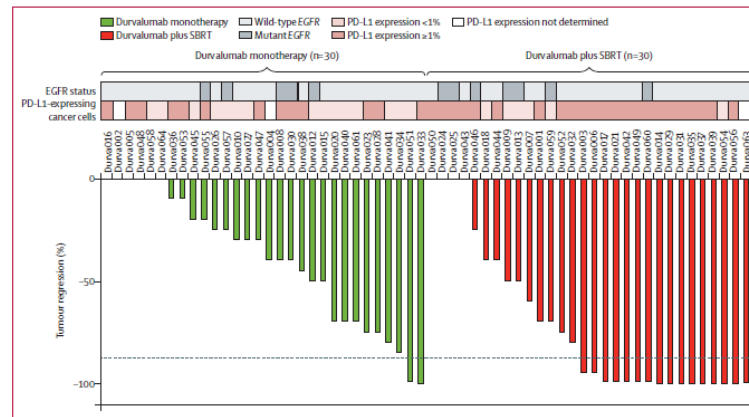


Weill Cornell Phase II RCT:

- Stage I-IIIa NSCLC
- n=60
- Neoadjuvant durvalumab +/- sub-ablative RT (8 Gy x 3)
- Major PR observe in 6.7 vs 53.3% of cases
- Combined therapy well tolerated (G3+ toxicity: 17 vs 20%)
- Mediastinal downstaging higher in RT group (4/6 [66%] vs 1/7 [14%])

Neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small-cell lung cancer: a single-centre, randomised phase 2 trial

Nasser K Altorki, Timothy E McGraw, Alain C Barczuk, Ashish Saxena, Jeffrey L Port, Brendon M Stiles, Benjamin E Lee, Nicholas J Sanfilippo, Ronald J Scheff, Bradley B Piva, James F Gruden, Paul J Christos, Cathy Spinelli, Joyce Gakuria, Manik Uppal, Bhavneet Binder, Olivier Elemento, Karla V Ballman, Silvia C Formenti

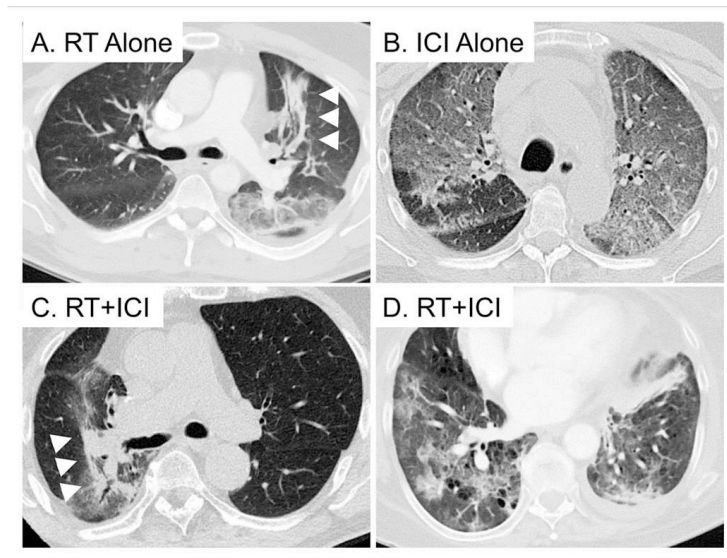




Treatment Related Toxicity with RT in immunotherapy Era

New Challenges:

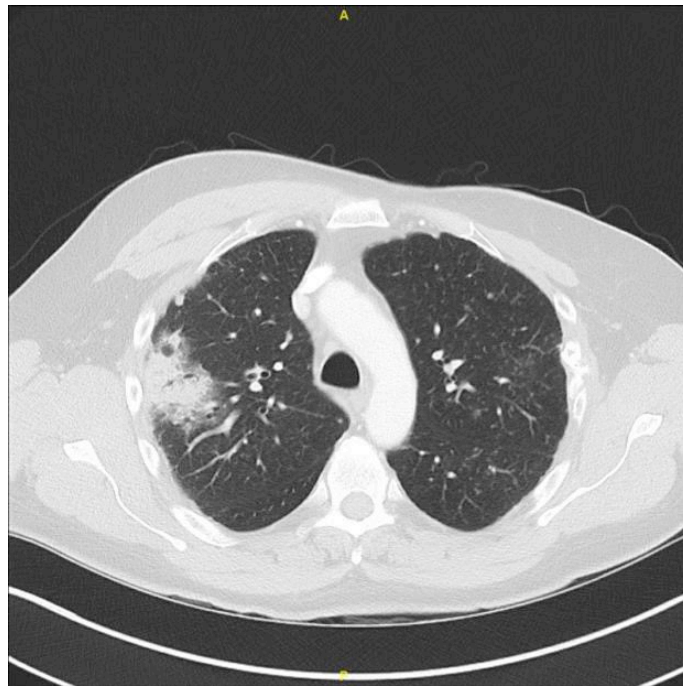
- Diagnosis
- Treatment





Louie et al. Delphi Consensus

- General: Important to recognize ILD (including sub clinical ILD) up front
- Diagnosis: Involve Rad Onc, CT Chest. Consider: PFTs, bronch
- RT Optimization
- Treatment: Steroids, Holding adjuvant therapy





THANK YOU

