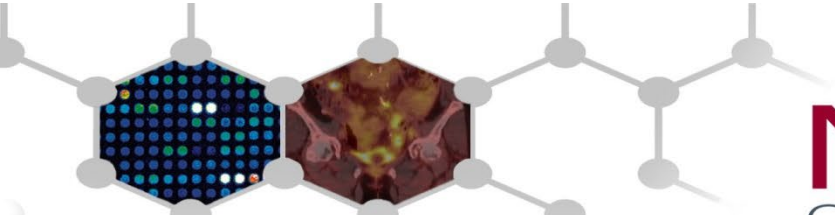

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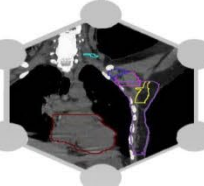


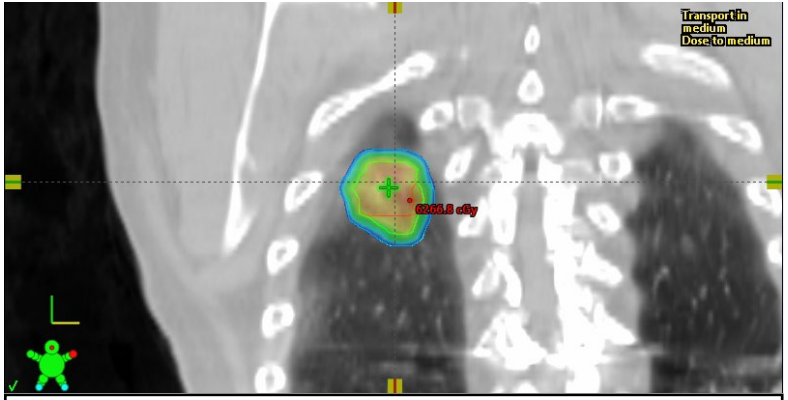
PACIFIC 4 / RTOG 3515

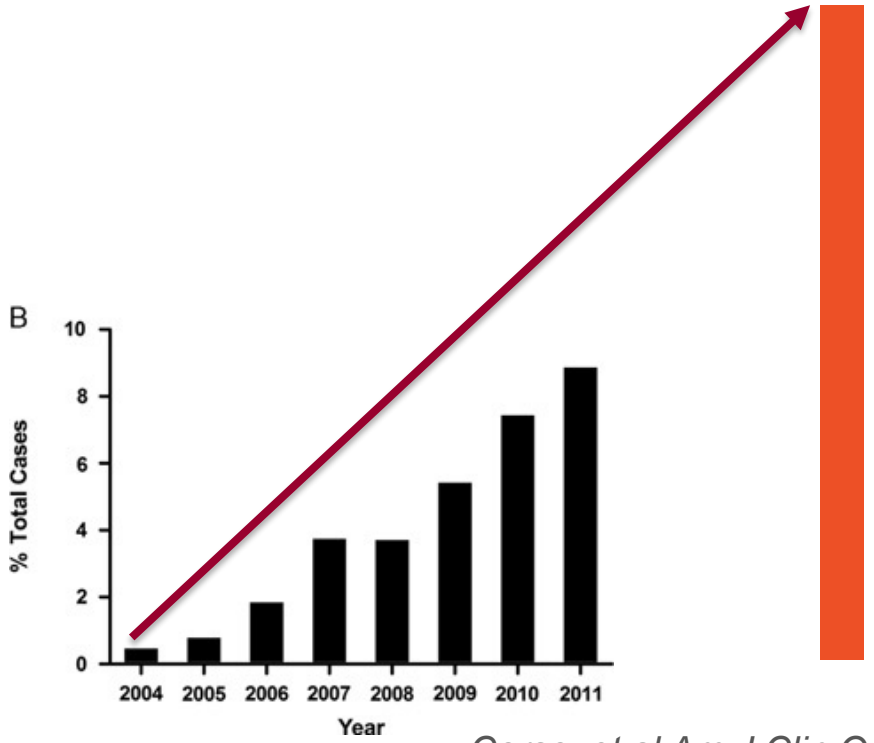
Cliff Robinson, MD (PI)
Washington University in St. Louis

@SBRT_CR

NRG Summer 2022 Lung Committee

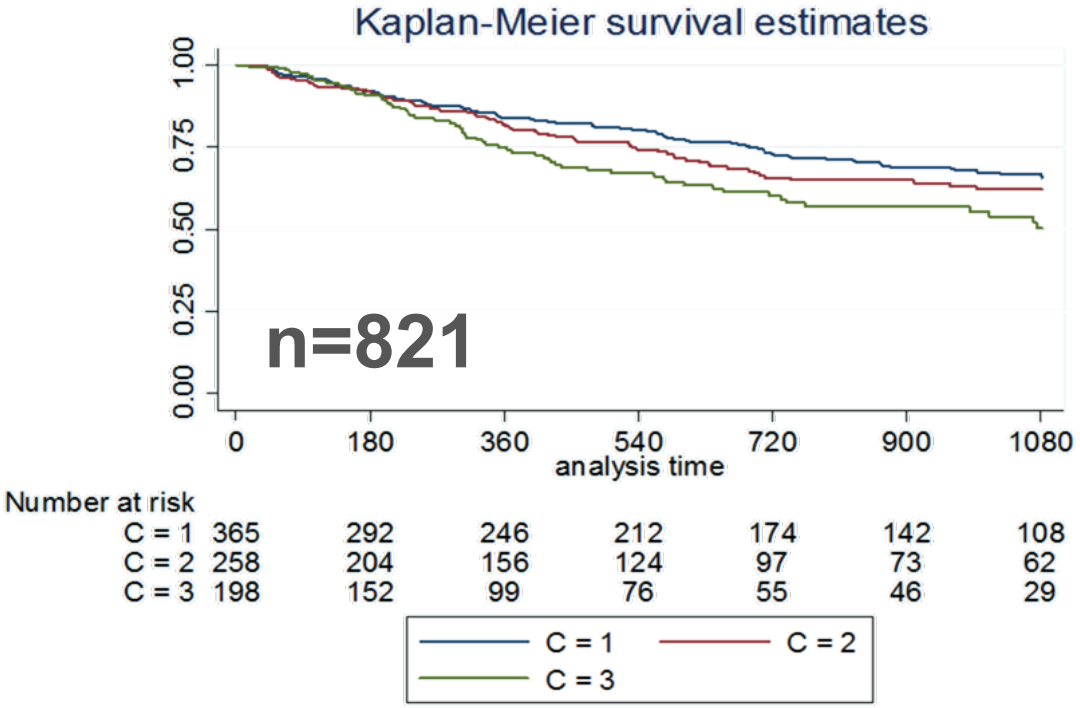
Increasing Use of SBRT for Early NSCLC





Corso, et al Am J Clin Oncol 2017
Jang, et al ASTRO 2019

SBRT Failures Increase With Size



Freedom from First Failure (Death Competing Risk)			
	1y	2y	3y
<=2 cm	80.3	69.1	**62.8**
>2-3 cm	74.1	65.1	**60.2**
>3-7 cm	67.2	56.9	**51.1**

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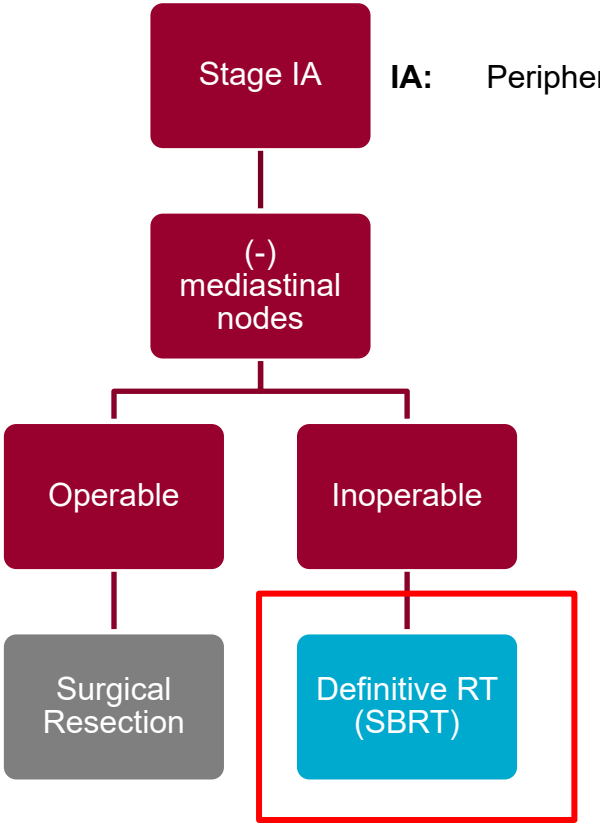
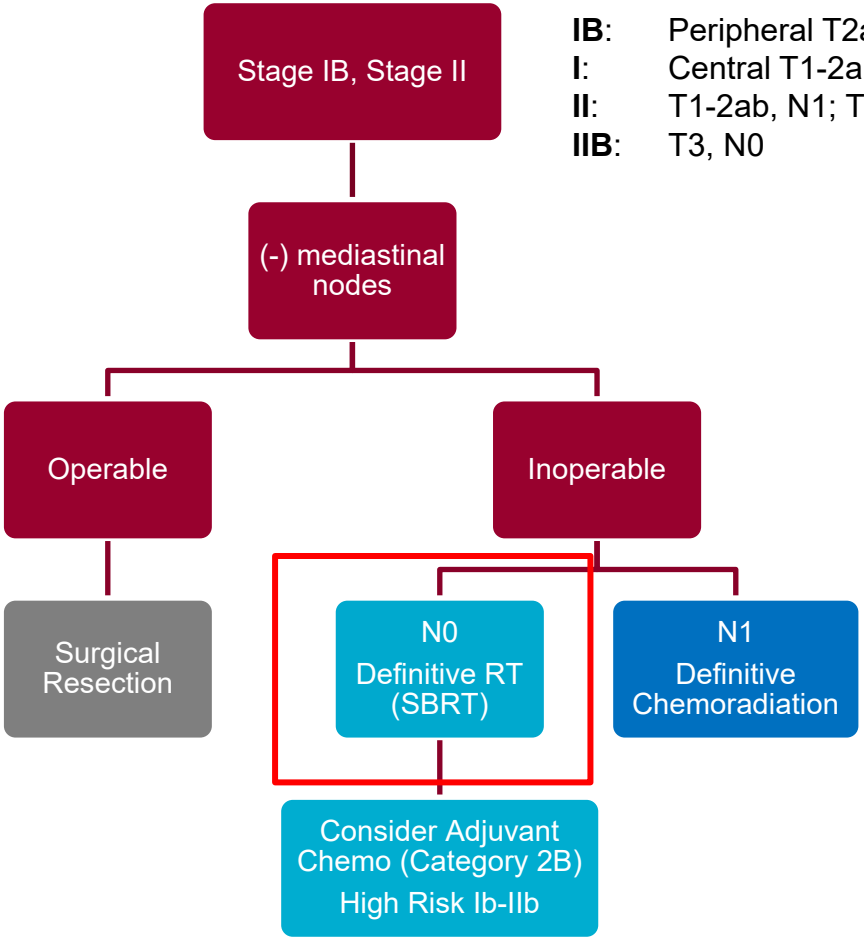
Washington University - Unpublished

NCCN Guidelines - NSCLC



IA: Peripheral T1abc, N0

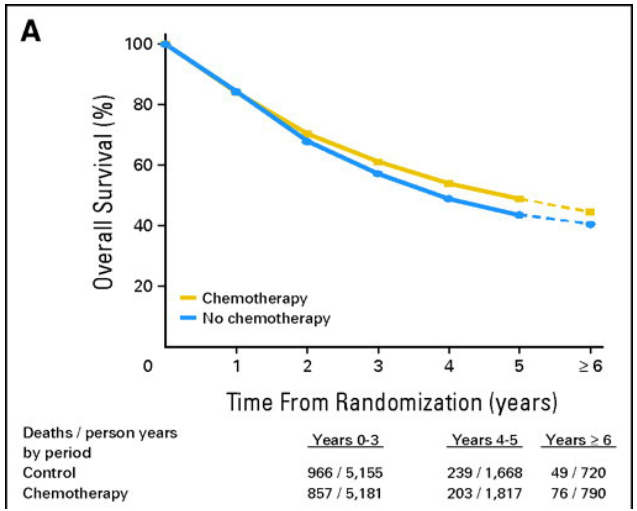


IB: Peripheral T2a, N0
I: Central T1-2a, N0
II: T1-2ab, N1; T2b, N0
IIB: T3, N0

Adjuvant therapy after SBRT?

Pignon et al, JCO 2008

N=4,584



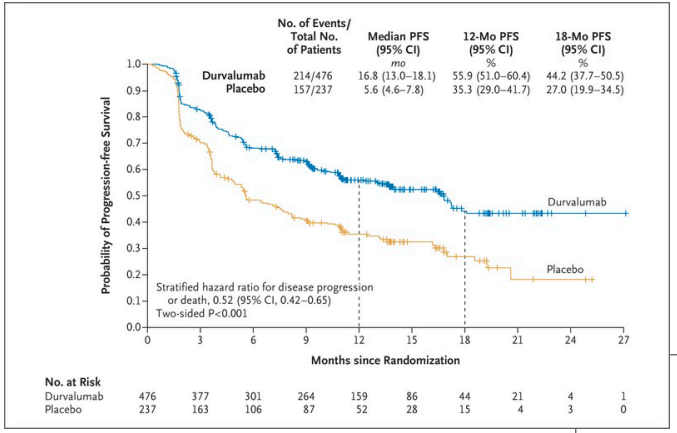
Deaths / person years by period	Years 0-3	Years 4-5	Years ≥ 6
Control	966 / 5,155	239 / 1,668	49 / 720
Chemotherapy	857 / 5,181	203 / 1,817	76 / 790

5y OS improvement 5.2%, no clear benefit for IA/IB

- Cytotoxic chemo NCCN Category 2B rec for “high risk” based on surgical data
- ***Challenging in frail SBRT population. . .***

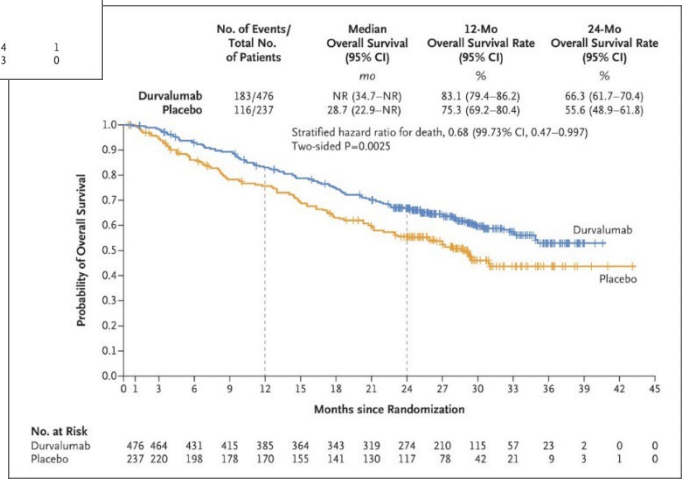
PACIFIC – CRT +/- durva for stage III

- **713 pts, 2:1** randomized
- **Durva** q2wk 10 mg/kg or placebo up to 12 mo
- **PFS** 17.2 mo vs. 5.6 mo
- **OS** NR vs. 28.7 mo
- **Well tolerated**
  - G3/4 AEs – 30.5% vs. 26.1%
  - Pulmonary – 4.8% vs. 2.6%



mPFS 16.8 mo vs. **5.6 mo**

mOS NR vs. **28.7 mo**



Antonia et al, NEJM 2018

RT + IO

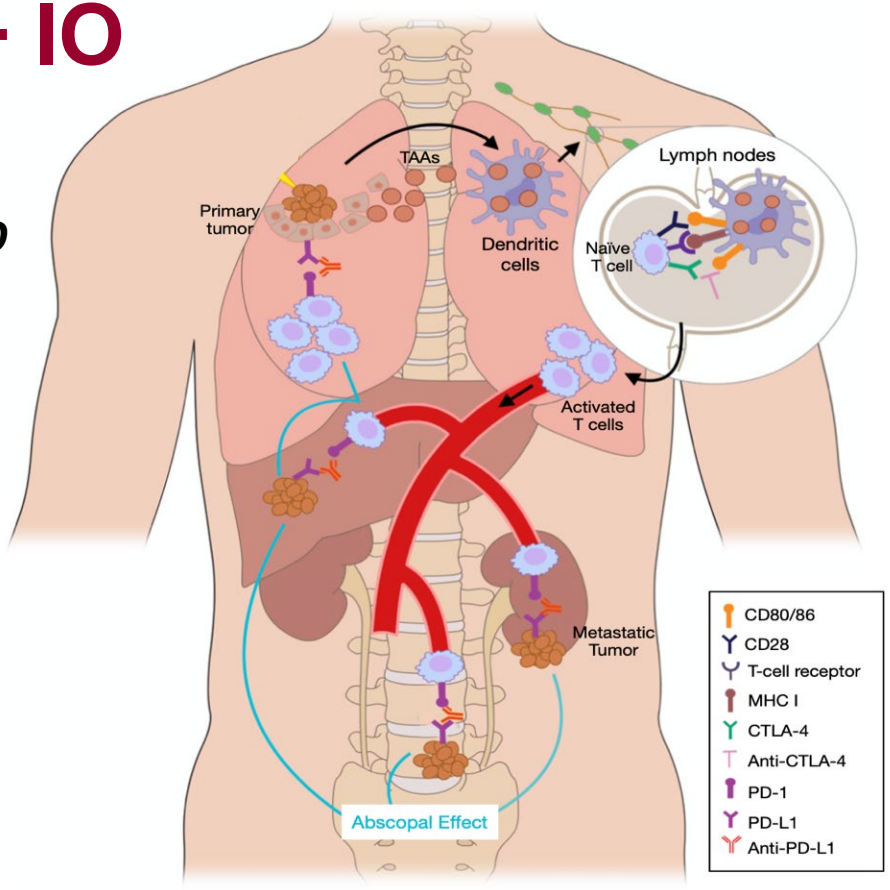
Increasing evidence of synergy between RT + IO

<u>Potentiation</u>

- More immunogenic cell death
  - Larger fx size (SBRT) may increase antigen release and uptake
- Increased tumor infiltrating lymphocytes
- Upregulation of PD-L1 expression

<u>Cytoreduction</u>

- Relieve immunosuppression



Chicas-Sett et al; Cancers 2020, 12, 2178

Early Clinical Data Shows Safety Signal

iSABR (MDACC)

Chang et al, ASCO 2020

- rPh2
- **SBRT +/- nivo**
- SBRT w/nivo => nivo (4-7 total)

- N=>100/145 (*current*)
- 2xG2 RP, 1xG3 dyspnea
- No pt discontinue therapy from AE

iSABR (UCLA)

Lee et al (personal comm, recently closed)

- Ph1/rRh2
- **SBRT +/- durva**
- Durva x 1 => SBRT => durva (4 mo)

- Ph1 (N=15)
- No SAEs, DSM rec go to rPh2

UC Davis

Kelly et al, ASCO 2020

- Ph1/Ph2 expansion
- **SBRT + atezo**
- Atezo x 2 => SBRT w atezo => atezo x 3 (6 total)

- 3+3 (3mg/kg, 10mg/kg 1200 mg flat)
- Ph1 (N=15)
- 1xG3 rash DLT @ 10mg/kg
- RP2D 1200 mg, N=5
- No other SAEs to date

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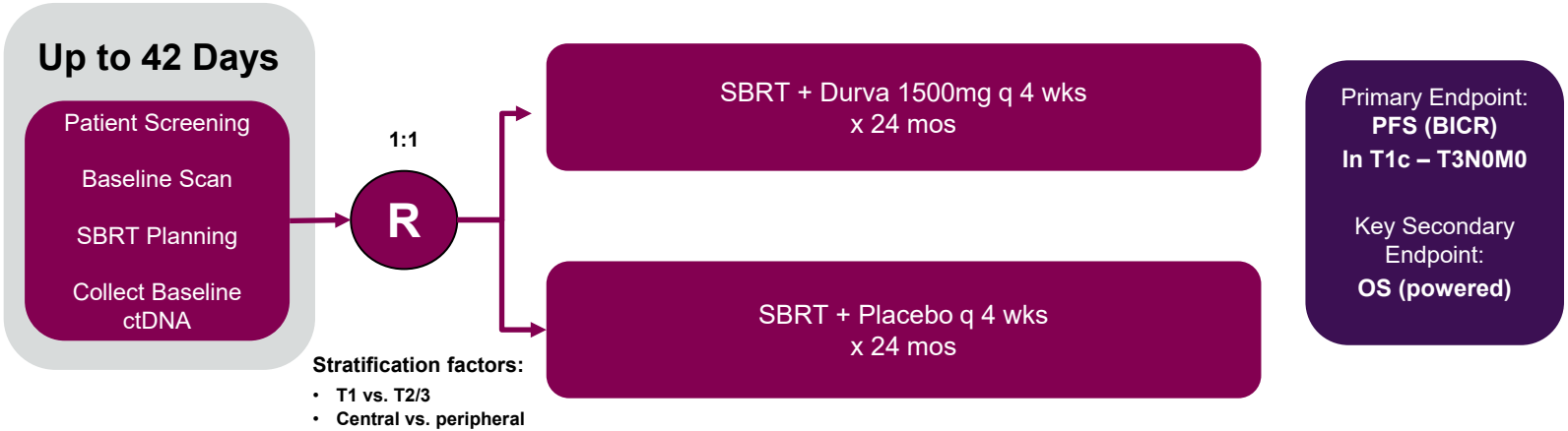
PACIFIC-4 / RTOG 3515 – v3

Inclusion Criteria

- Clinical Stage I/II node negative (T1 – T3 N0)
- Medically inoperable or refuse surgery
- ECOG PS 0-2
- All comers for histology and PDL-1 status
- ***Sync/Metach allowed***

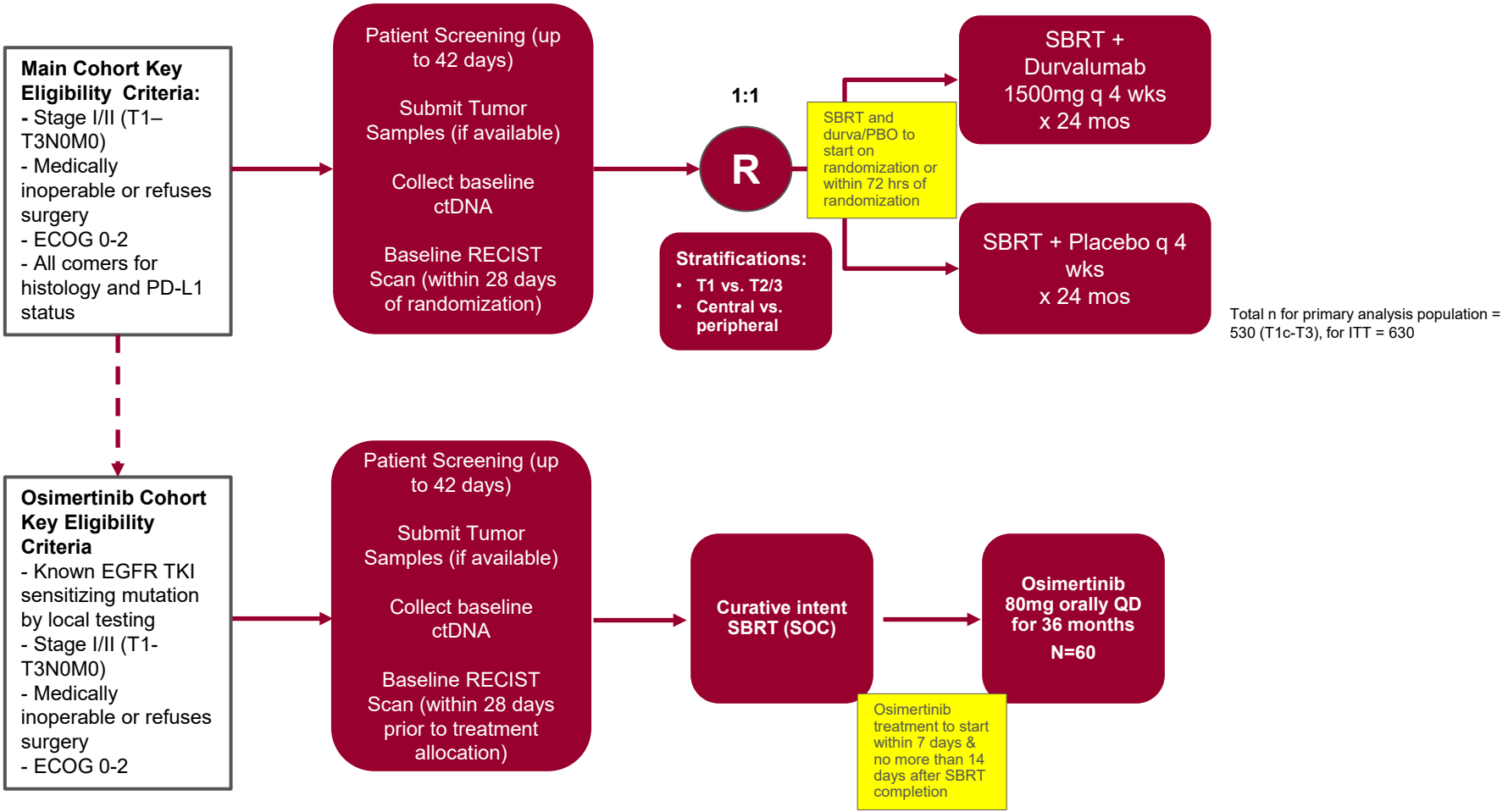


*Total n for primary analysis population = 530 (T1c-T3), Total n for ITT = 630

SBRT Dose Reflects Int'l Variability

50-60 Gy/8, 50-55 Gy/5
42-48 Gy/4, 54 Gy/3

PACIFIC-4 / RTOG 3515: Updated Design for CSPv4 onwards



>200 sites, 16 countries

07/12/22:
Screened – 605
Randomized – 408/630