

RT with CAR-T – Practical Application

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London

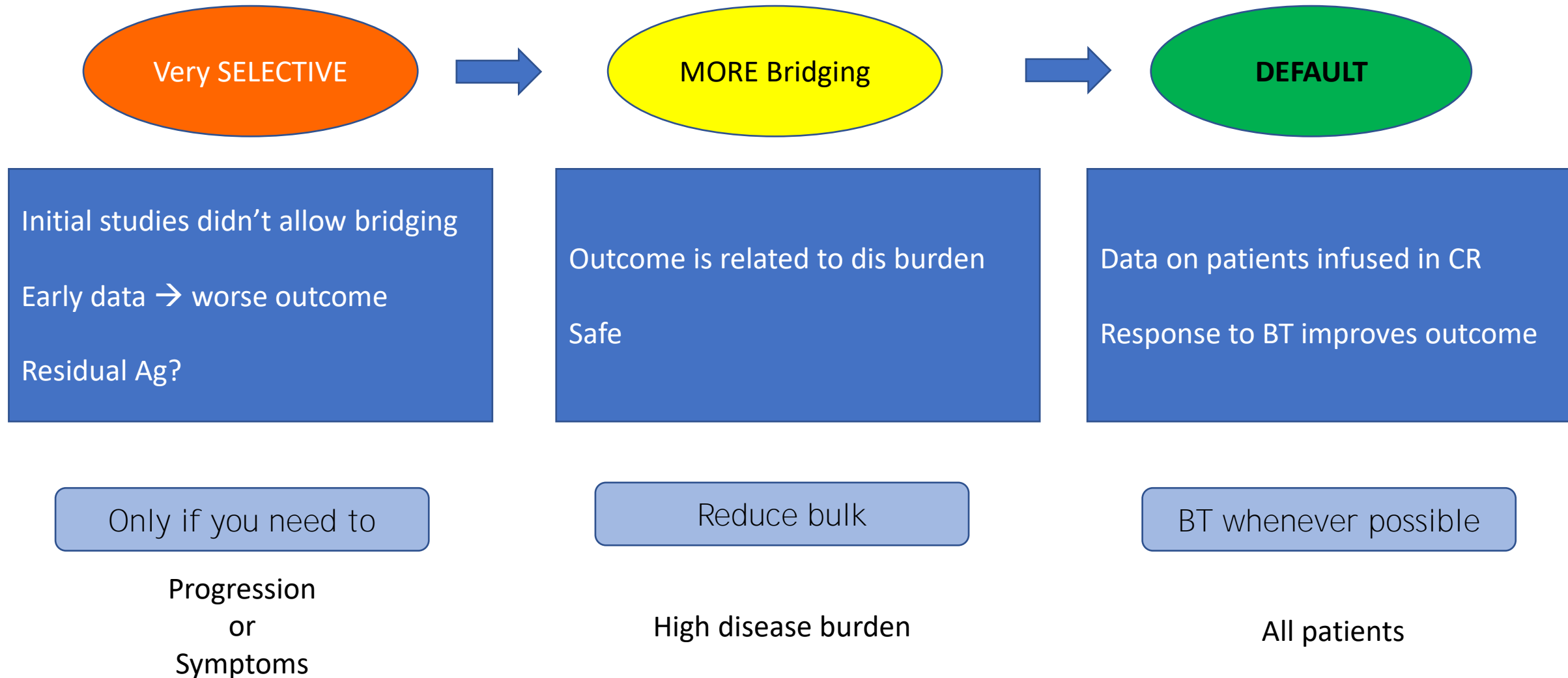
10.9.2023



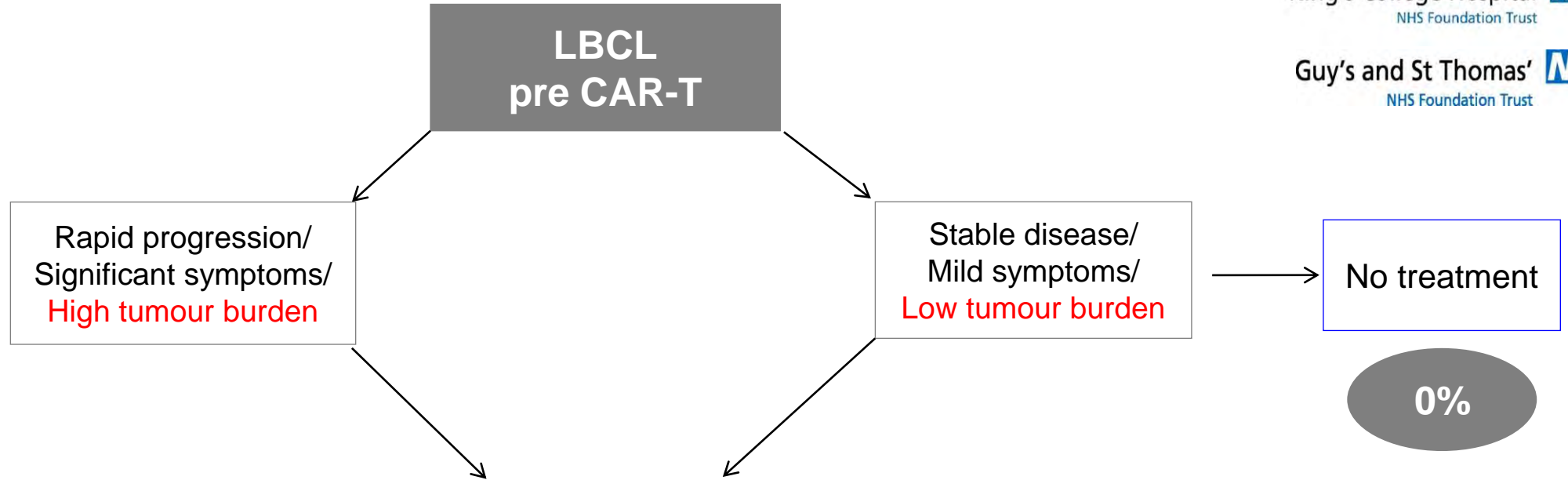
How to use RT with CAR-T: Practical Considerations

- Timing
- Dose / fractionation
- Volume
- Technique

Changing role of Bridging Therapy (BT)



Our current practice



Active debulking

- Rapidly progressive disease
- Wide-spread extra-nodal disease (e.g. liver, lung, bone, peritoneum)
- LDH >2xULN

RBP

70%

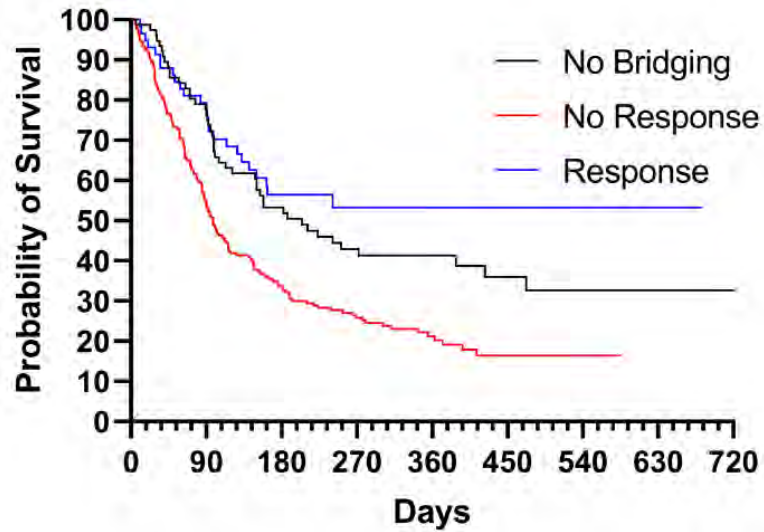
Radiotherapy

30%

Most areas can be covered by RT

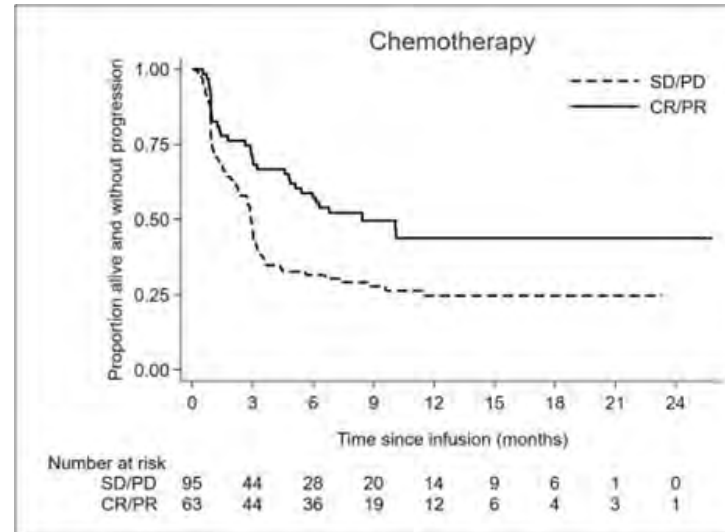
Response to bridging therapy matters

German RW cohort



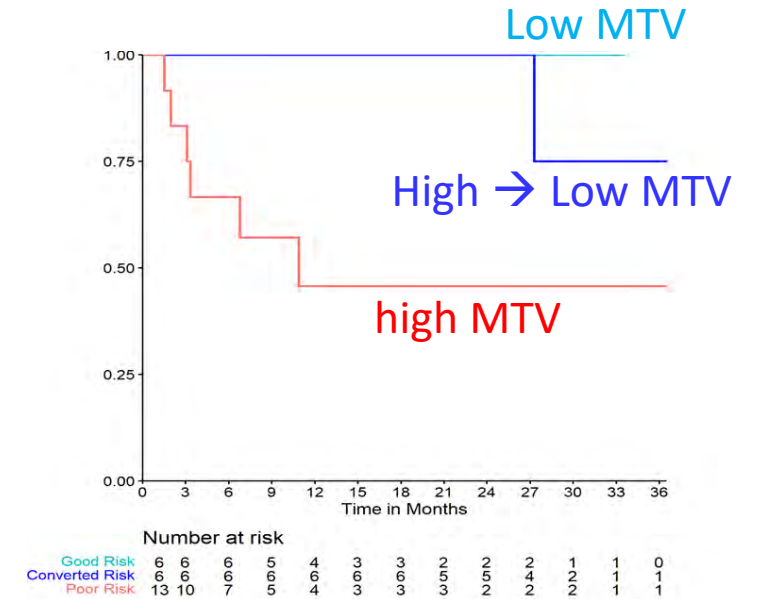
Bethke et al., Blood 2022

UK RW cohort



Roddie et al., Blood Adv 2023

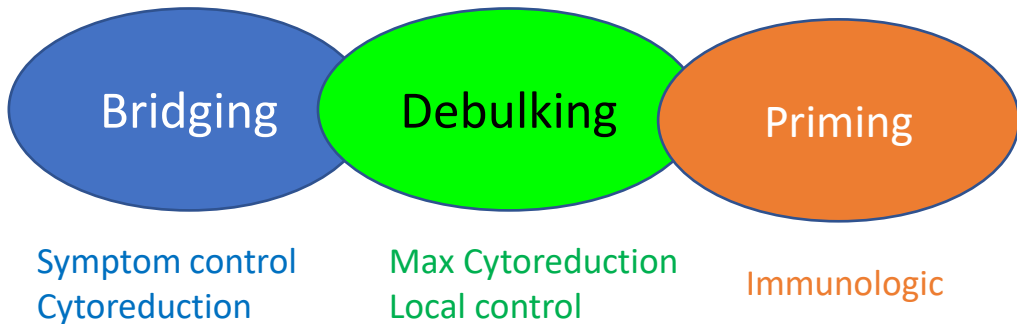
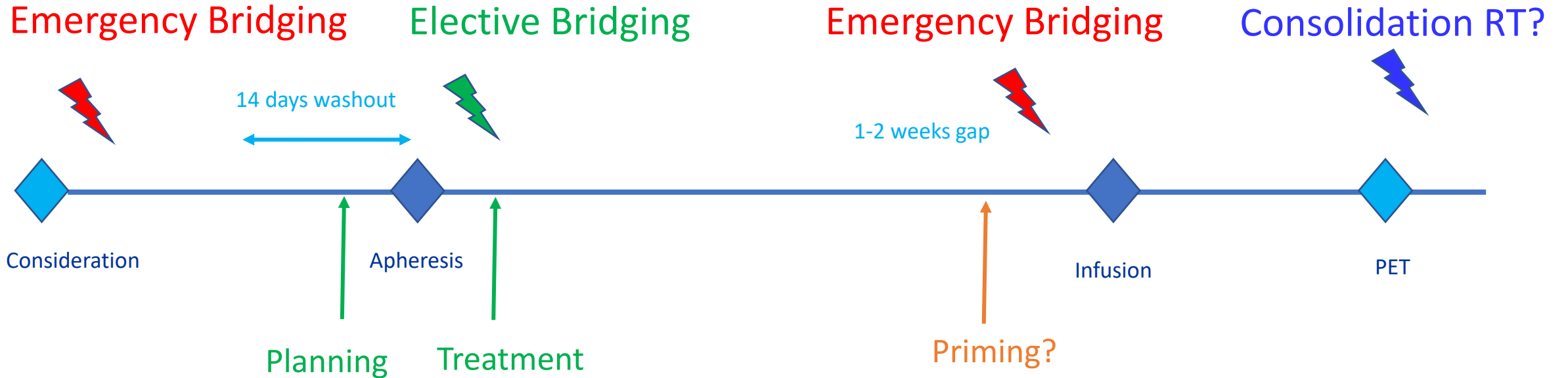
MSK study



Hubbeling et al., 2023

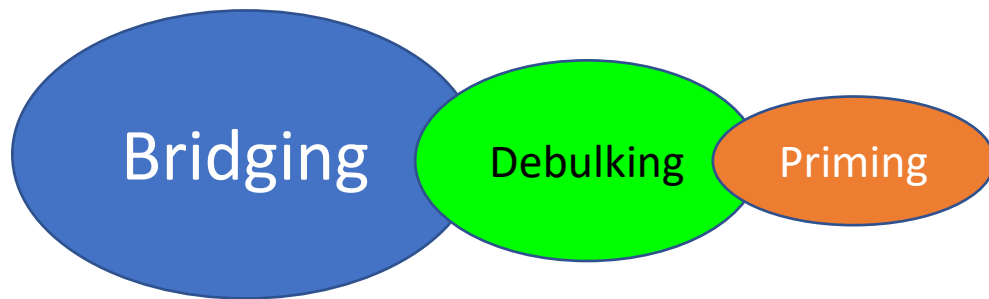
RW data: Debulking / Cytoreduction has clinical benefit

Different time of RT = different considerations & purposes



- Dose / fractionation
- Volume
- Technique

Emergency Bridging



- Short window
- Volume: progressive / symptomatic lesion
- Dose: EQD2 = 20-30 Gy
- Hypofractionation
- Technique: what is feasible

Emergency RT before CART

- 51y fit business man, **DH DLBCL**:
 - R-DA-EPOCH x6
 - MATRix x4
 - IVE x1
 - ESHAP x1 + IT-MTx
- **CAR-T next week**

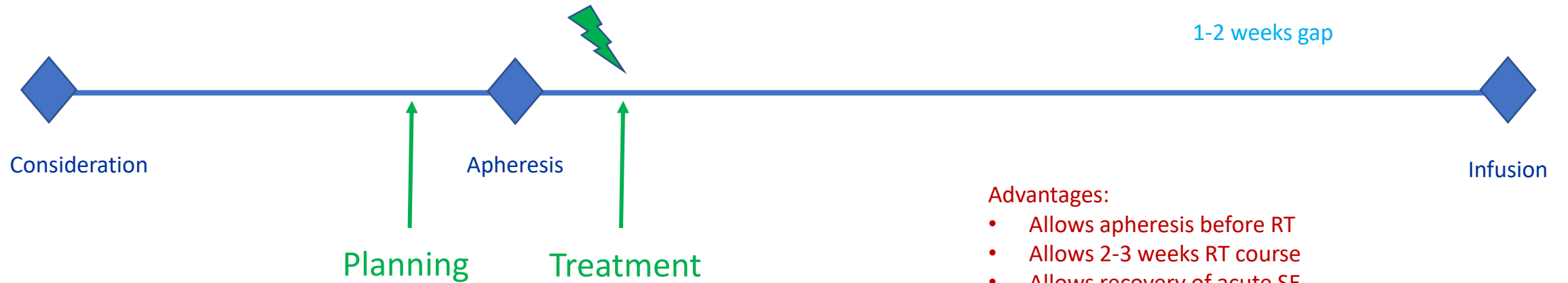


20Gy / 5#



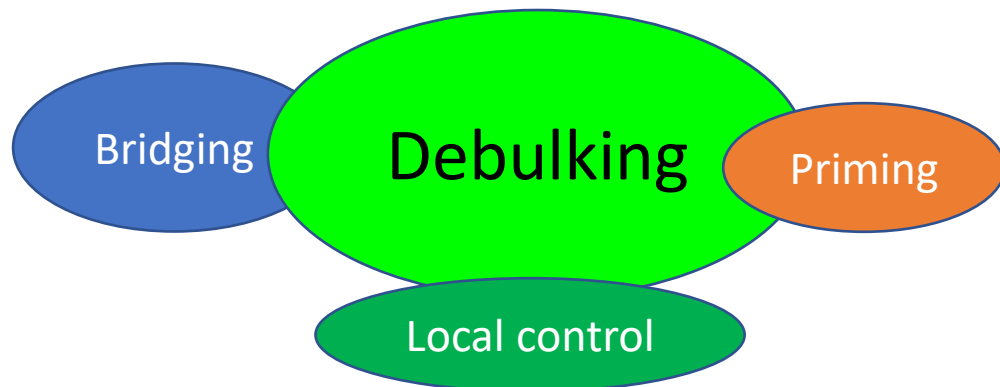
Post CAR-T

Elective Bridging



Advantages:

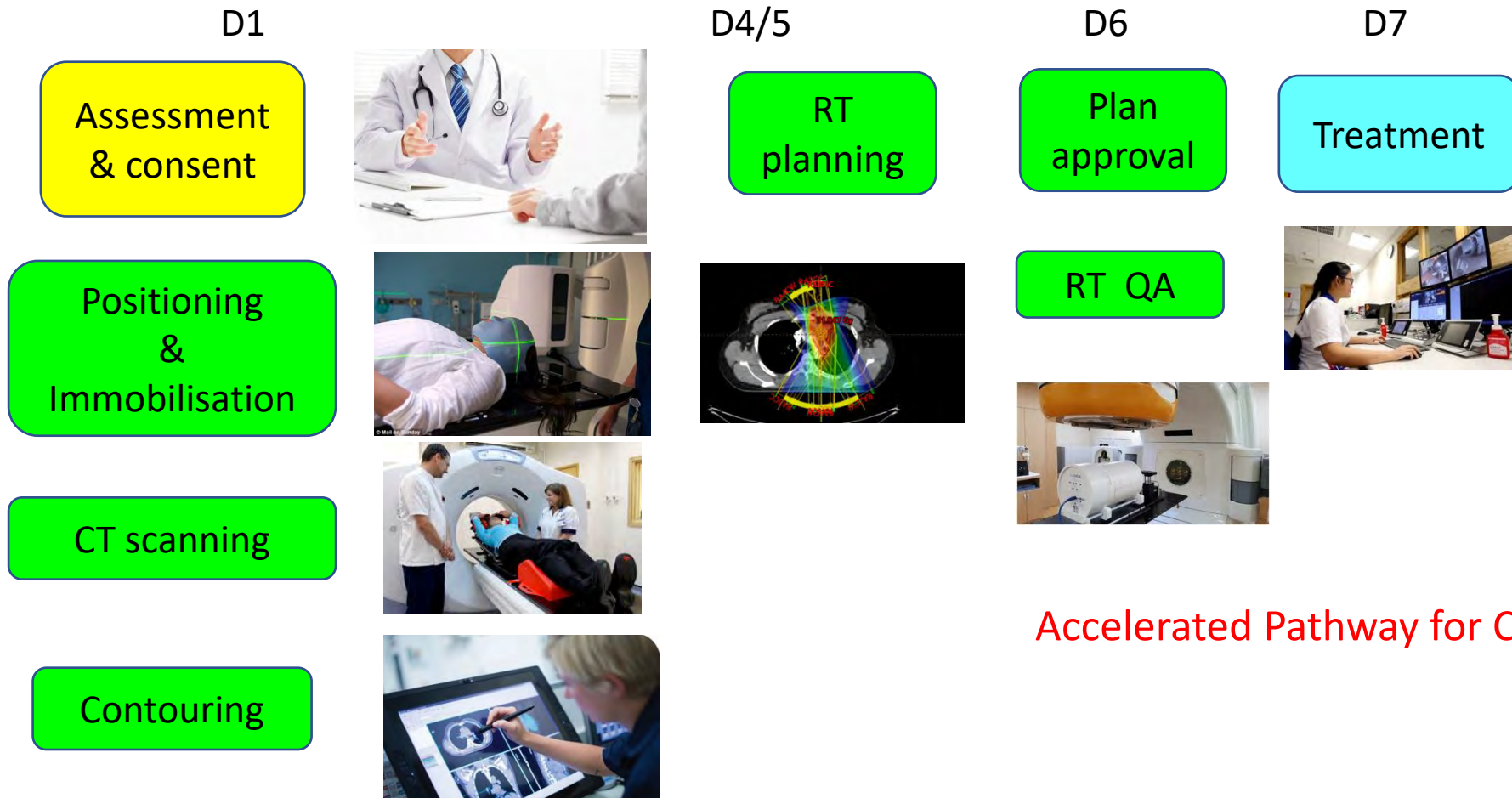
- Allows apheresis before RT
- Allows 2-3 weeks RT course
- Allows recovery of acute SE



- Long window
- Volume: as **comprehensive** as possible
- Dose: EQD2 = 30-40 Gy
- **2 dose levels?**
- Technique: high precision

Planned Pathway:

- Identify RT patients at **CAR-T decision** (even before NCCP)
- Pre-book accelerated RT pathway – aiming for RT to start after apheresis



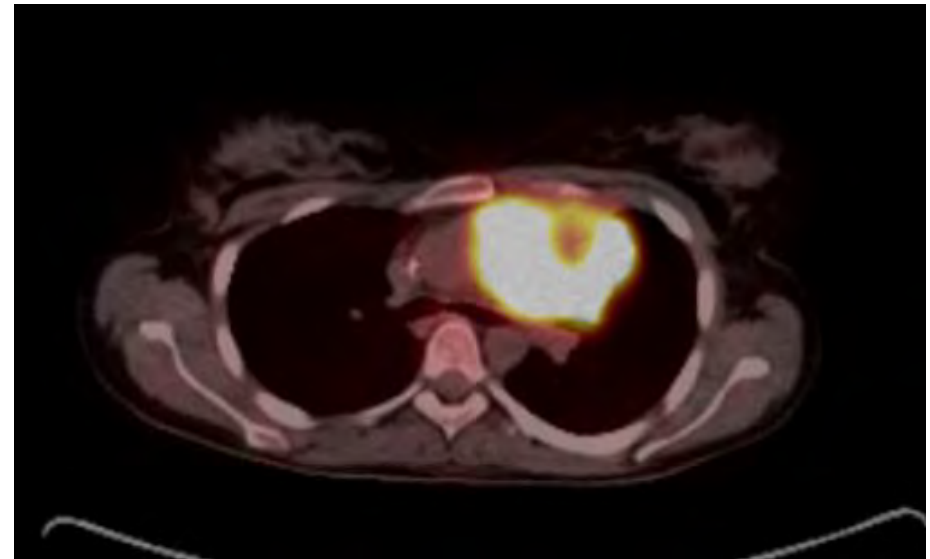
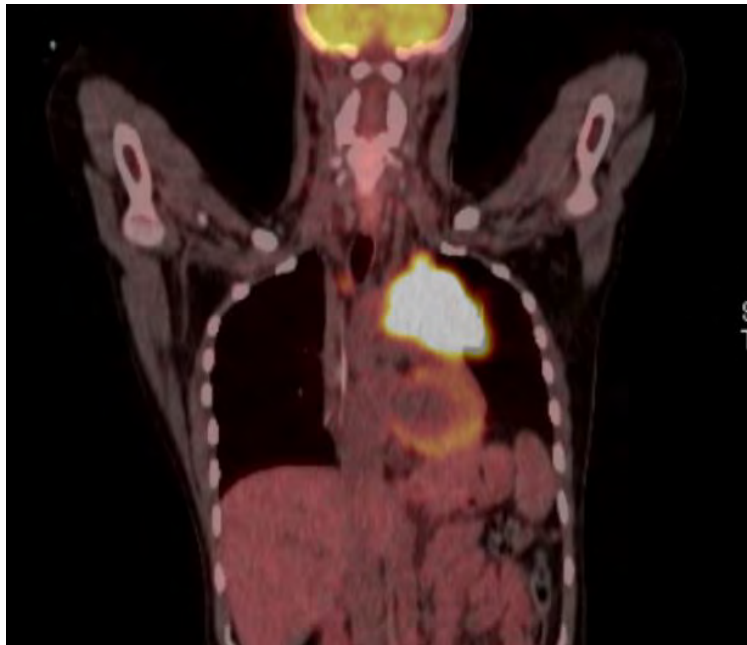
Accelerated Pathway for CAR-T

Elective bridging RT before CART

20 y.o. female

PMBCL, Refractory to 1st and 2nd line chemo → waiting CAR-T

Chest and L arm symptoms progressing rapidly





date referred	date seen	date scanned	date countoring	plan approval	start date	end date
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12/09/2019	13/09/2019	13/09/2019	13/09/2019	19/09/2019	23/09/2019	11/10/2019
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D1

D2

D8

D12

D30

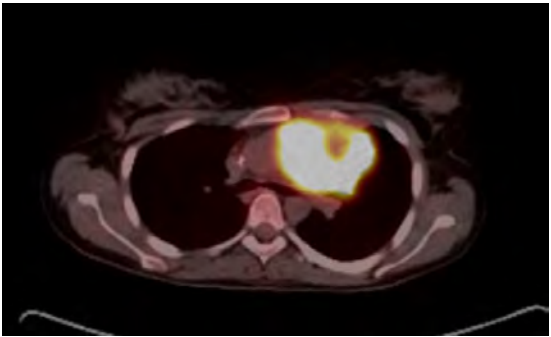
30 Gy / 15#

Apheresis

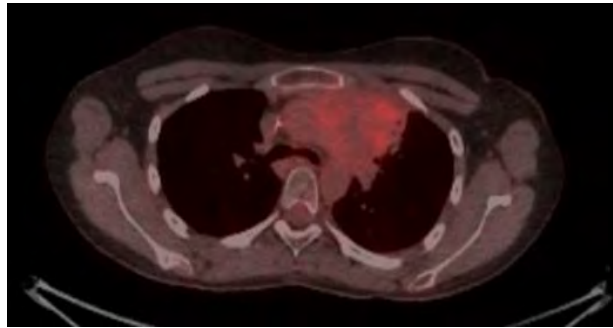
CAR-T

24/10/2019

Vein-to-vein = 32 days



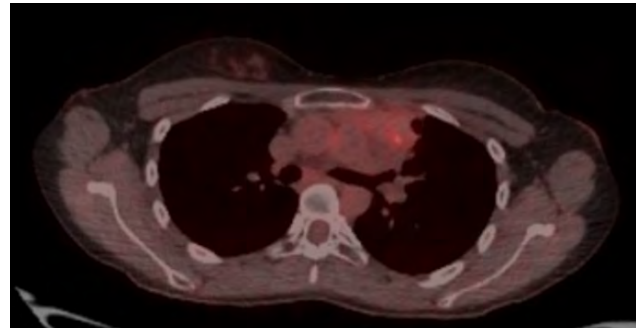
Pre-RT



Pre-infusion

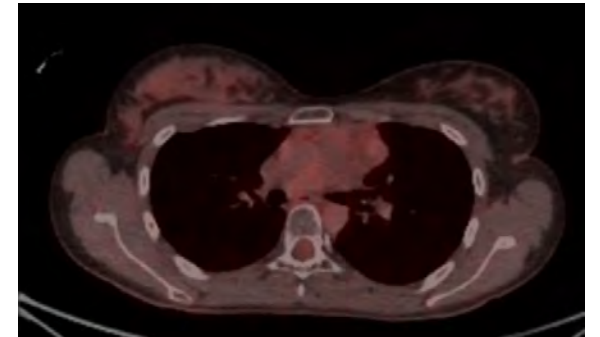
10 days > RT

PMR: DS-4



Month 6:

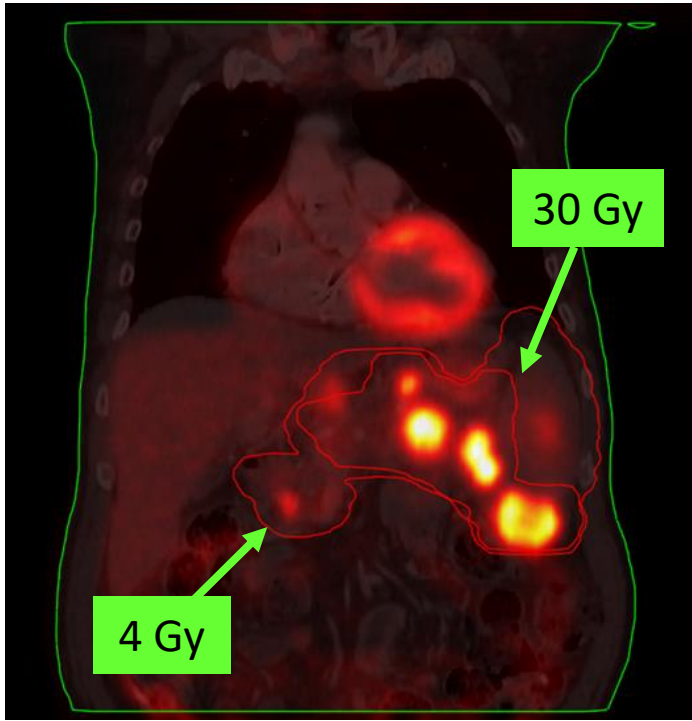
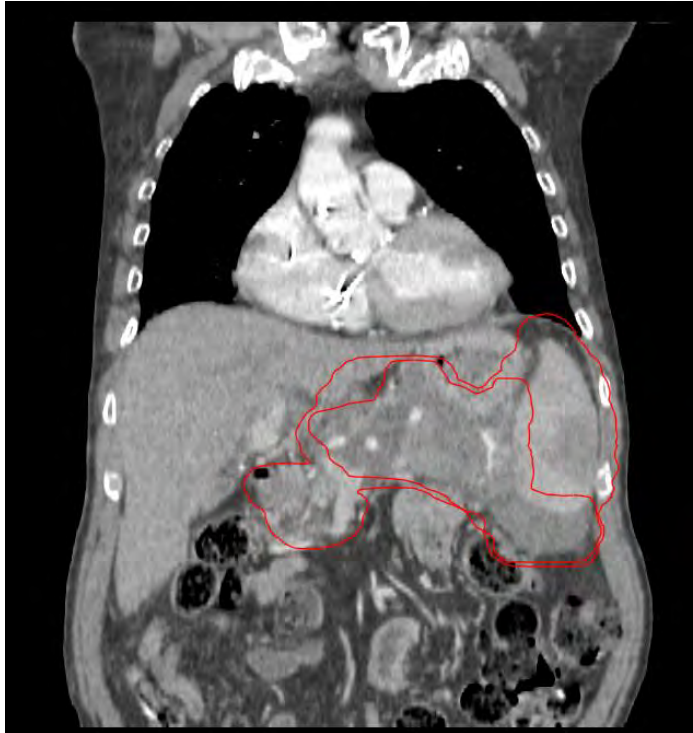
CMR: DS-3



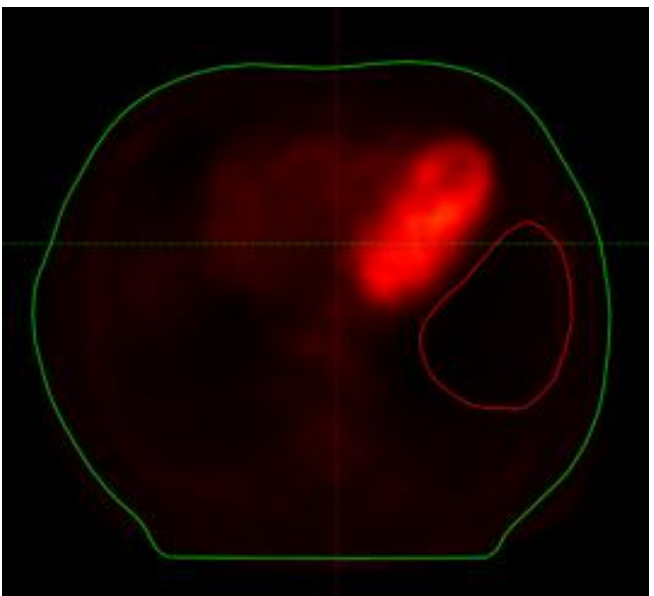
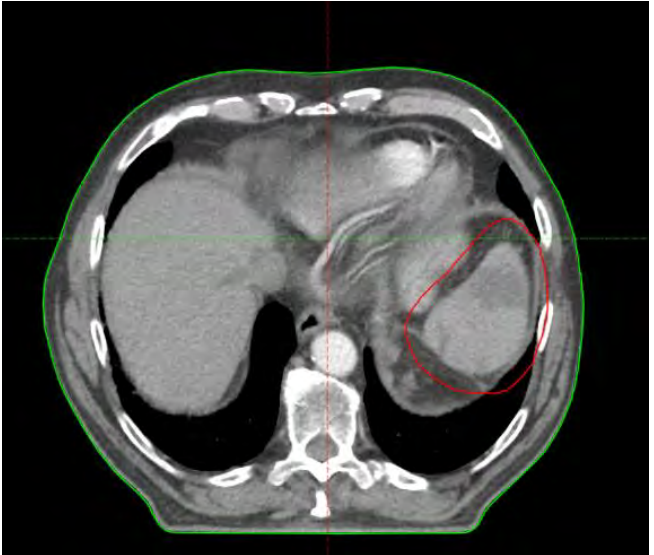
Month 12:

CMR: DS-2

2 dose levels



30 Gy then 4Gy



Stage 4, multiple sites

68 yo female

DLBCL

2nd relapse, 18m > autograft

Stage 4

High LDH

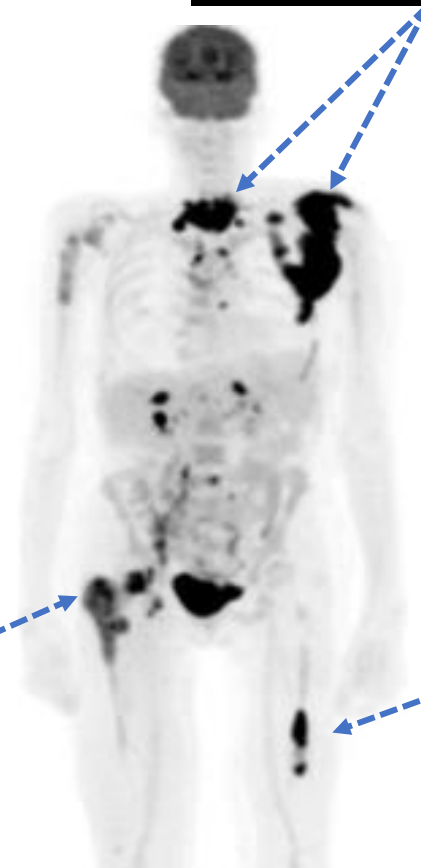
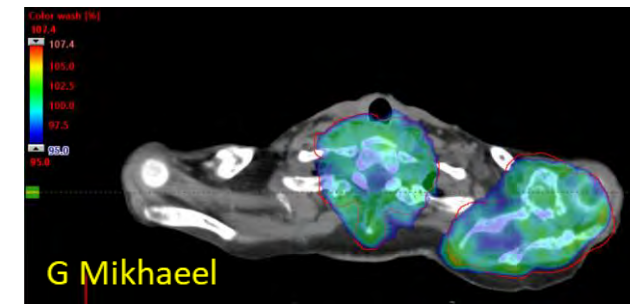
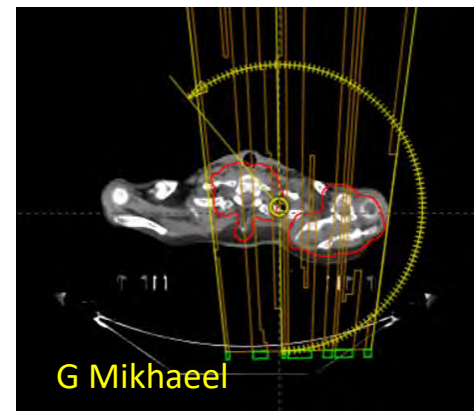
PS 1

Symptoms:

Pain + reduced mobility L shoulder

Pain R hip

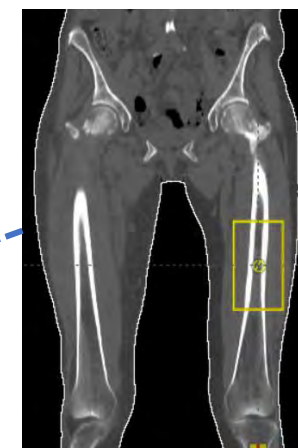
Radicular pain R arm



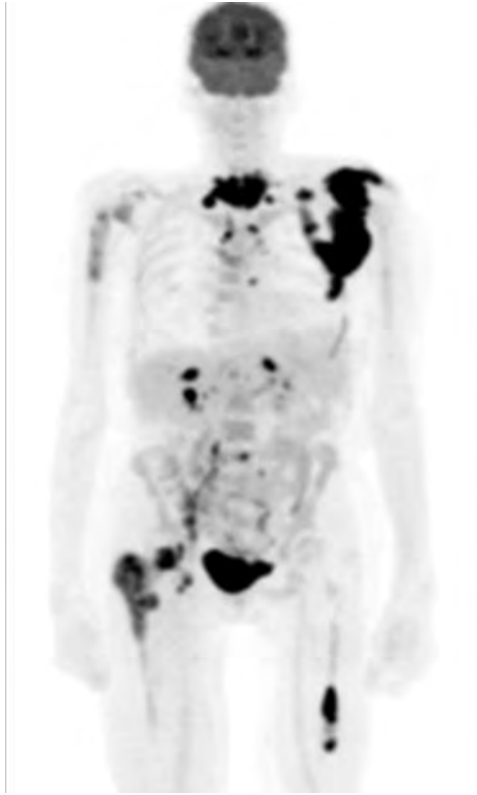
- 1) L shoulder 20Gy/10#
- 2) C7-T1 20Gy/10#



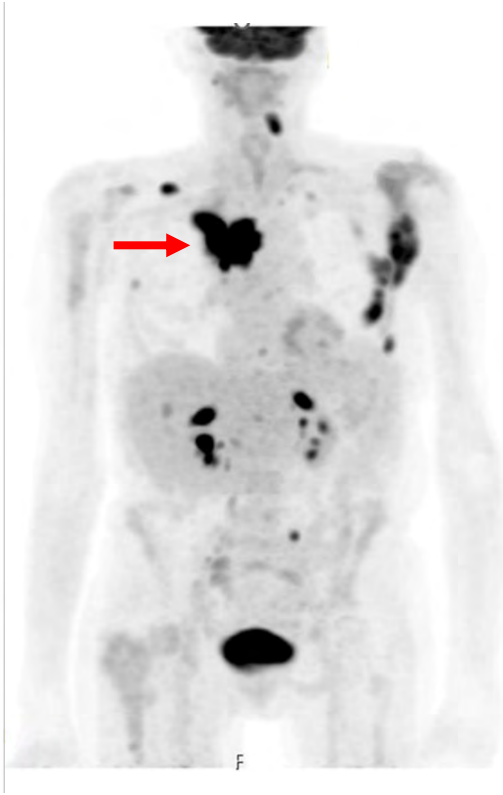
- 3) R hip 20Gy/10#



- 4) L mid-femur 4Gy/2#



**Before
Bridging**



**Pre-Infusion (Tisa-cel)
(10 days > RT)**

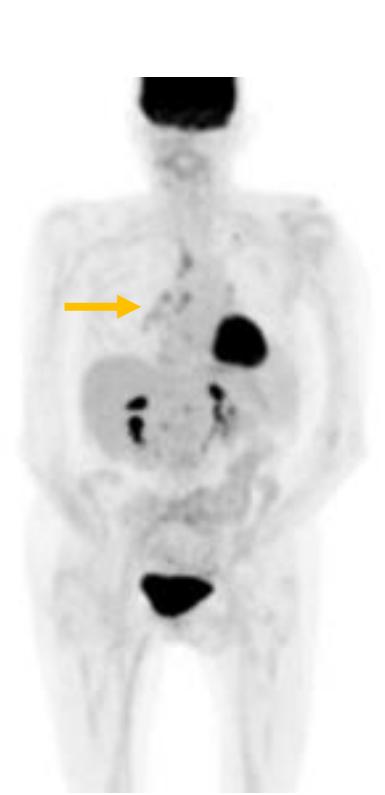
In-field PR
Out-of-field PD



**Month 1:
DS-4 in RT site**



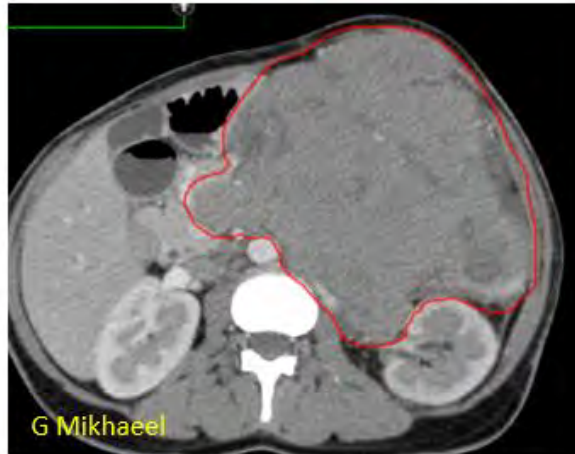
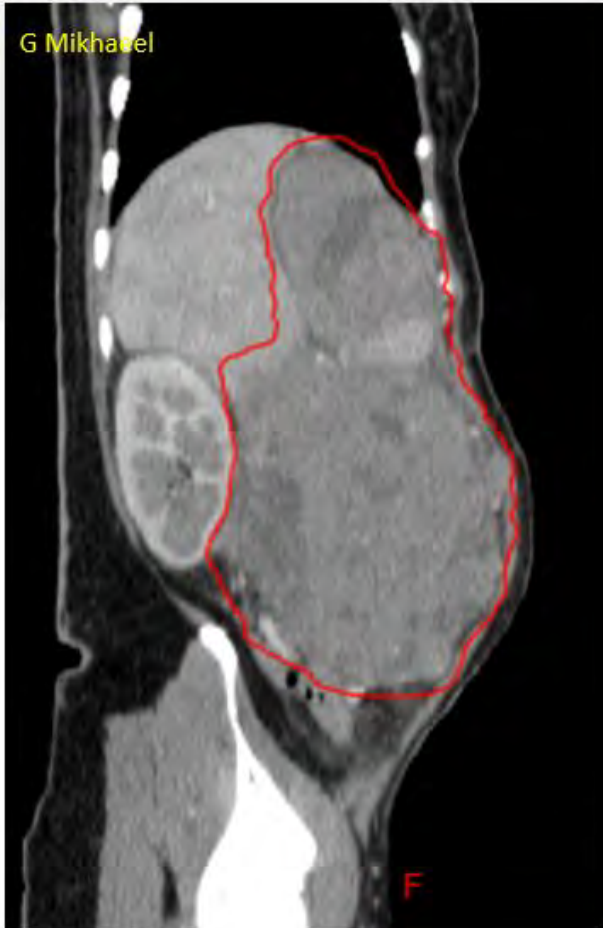
**Month 3:
DS-4 in RT site
(reduced)**



**Month 6:
CMR in previous sites
+ ?Sarcoid reaction**

Do we always have to fit within the “window”?

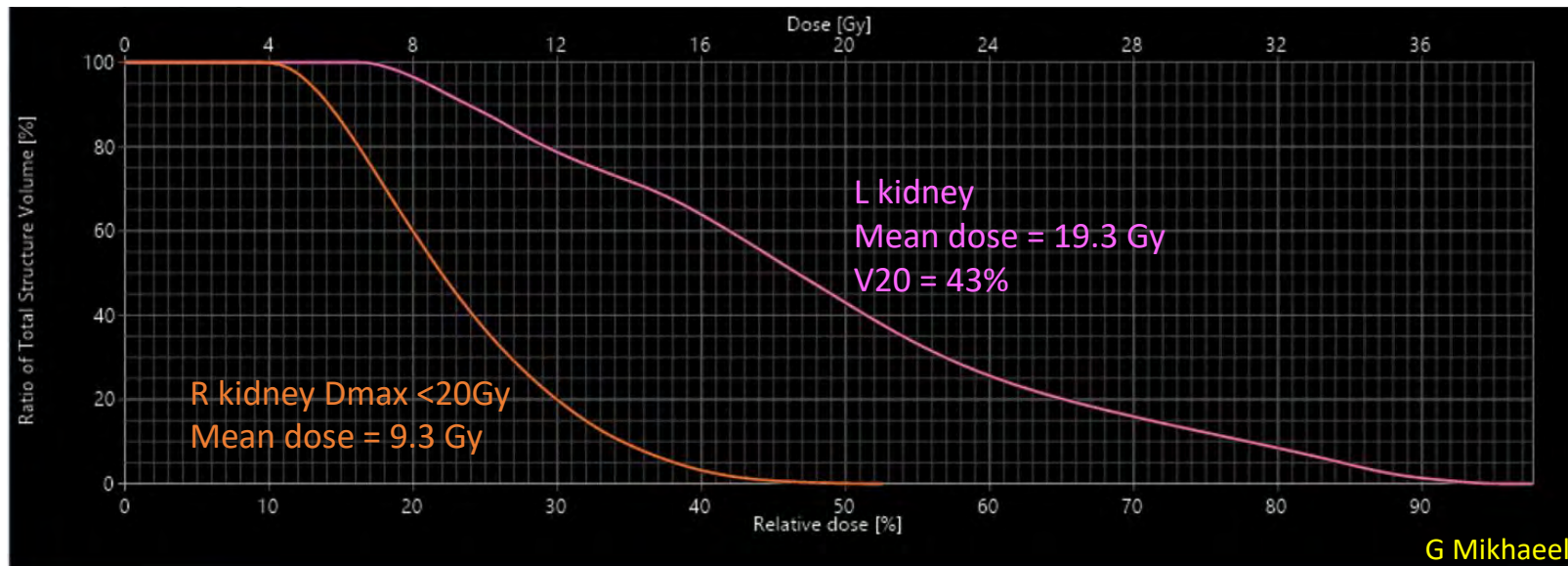
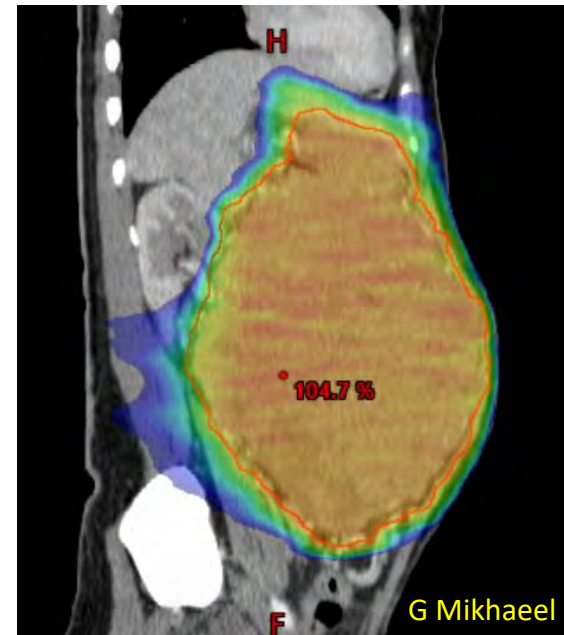
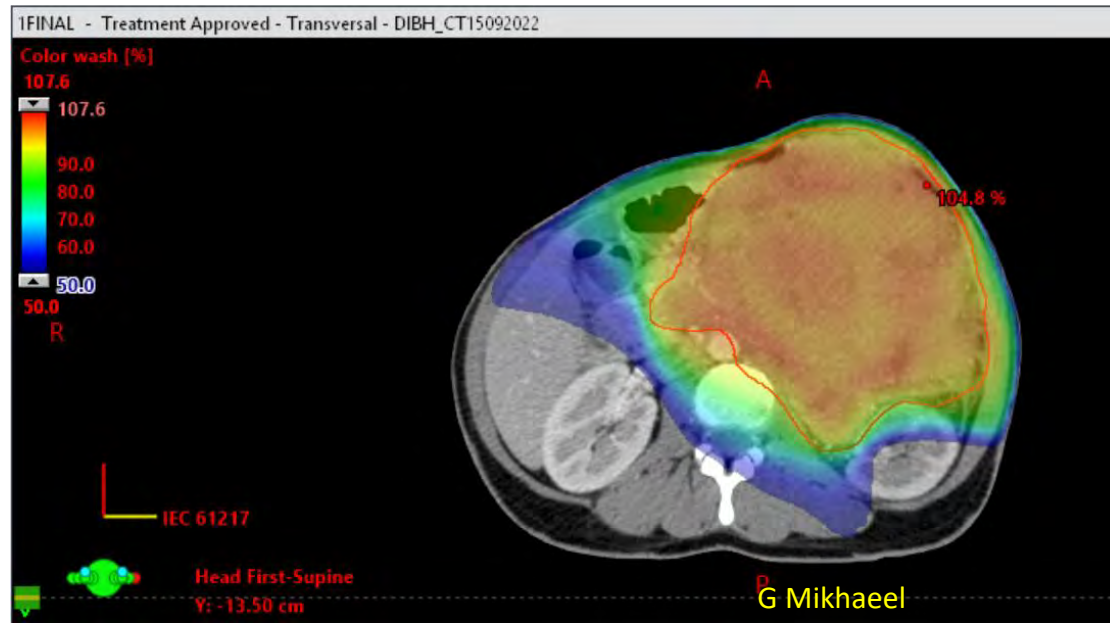
- 38 yo female
- DLBCL
- Treatment:
 - RCHOP x2: PD
 - R-Gem-Ox: PD
 - R-Pola-Benda: PD
- Approved for CART but: dis progressing: apheresis in 2 days
too bulky

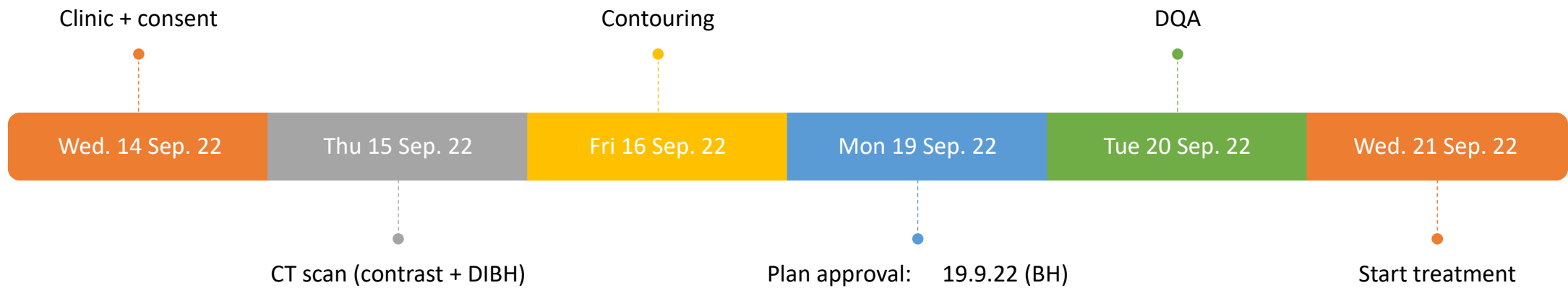


What would you do?

1. High-dose steroids
2. Short course RT **without delaying** CAR-T
3. Definitive dose RT & **delay** CAR-T
4. Abandon CAR-T

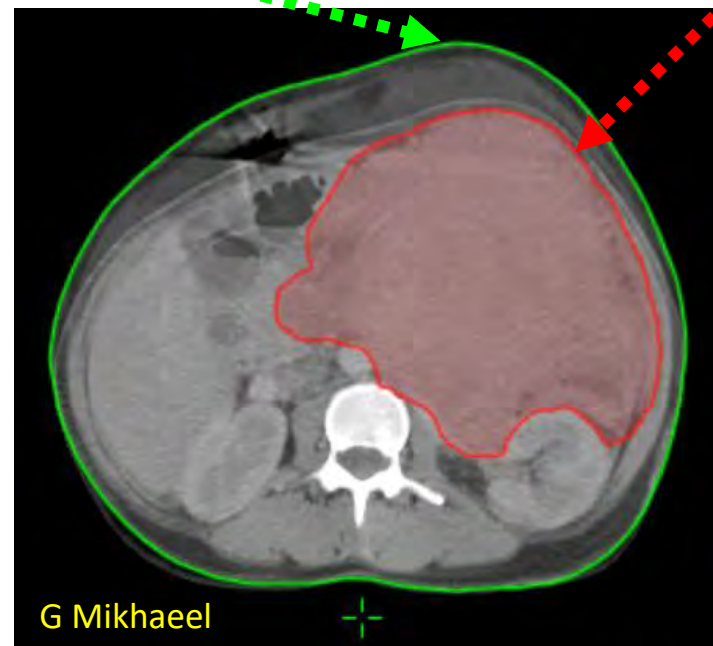
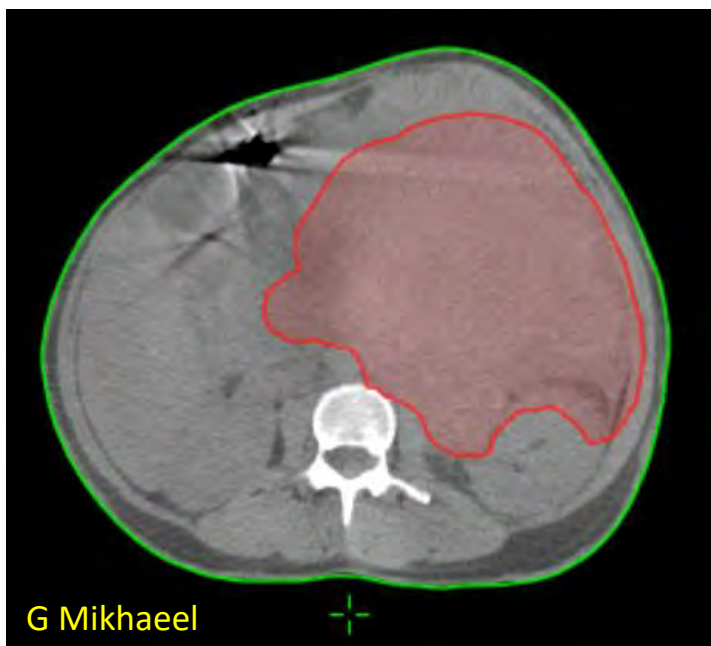
40Gy /20# /4wks

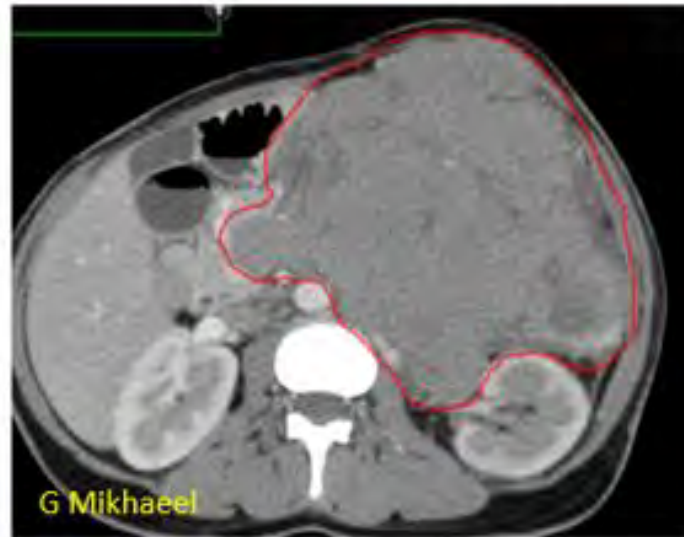




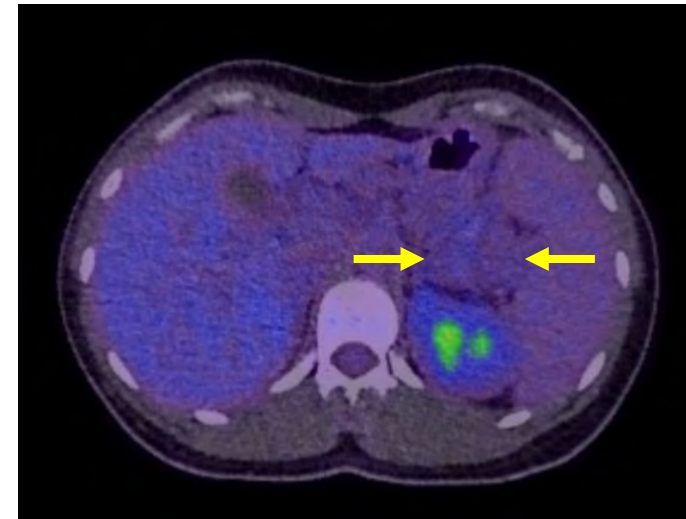
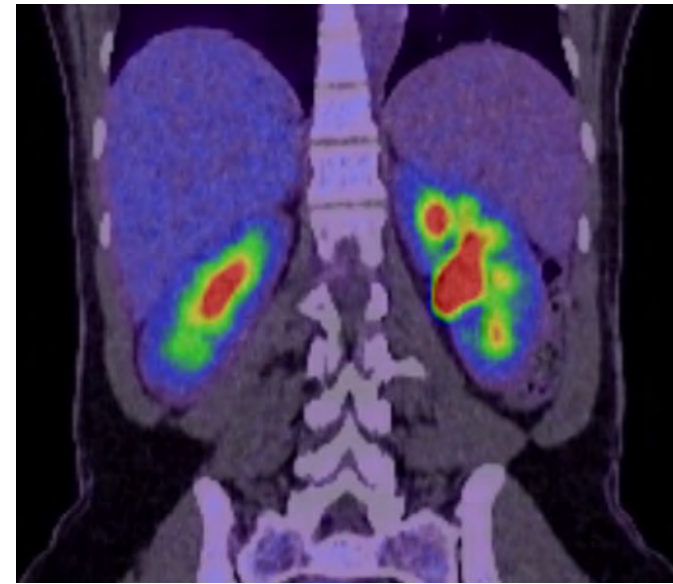
CBCT D1

Planning CT





Pre-RT



Month 6:

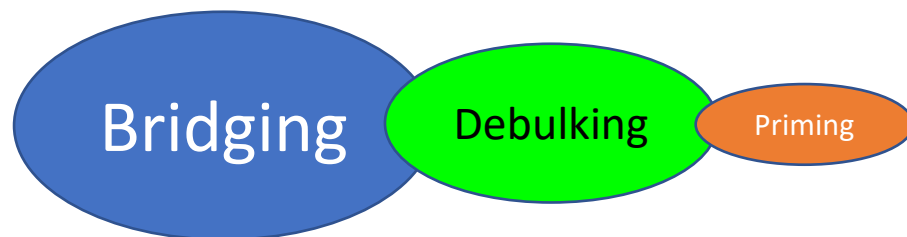
CMR: DS-3

Emergency Bridging



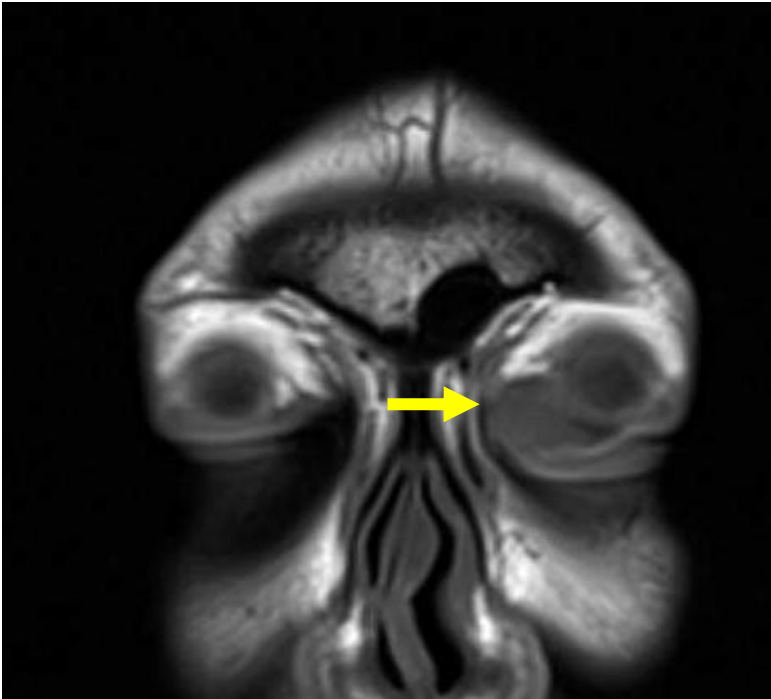
Indications:

- Spinal cord compression / airway obstruction
- Progressive / symptomatic dis, can't wait for apheresis



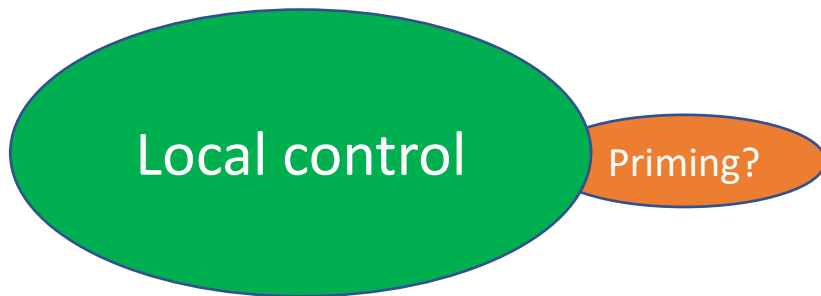
- Short window
- Volume: progressive / symptomatic lesion
- Dose: **lowest** needed
- \pm **more RT** > apheresis
- Technique: what is feasible

Emergency RT **before** apheresis?



- 8Gy/2#
- Allow longest gap possible to apheresis
- \pm more RT > apheresis
- Limited volume & avoid circulating blood

Different time of RT = different considerations & purposes

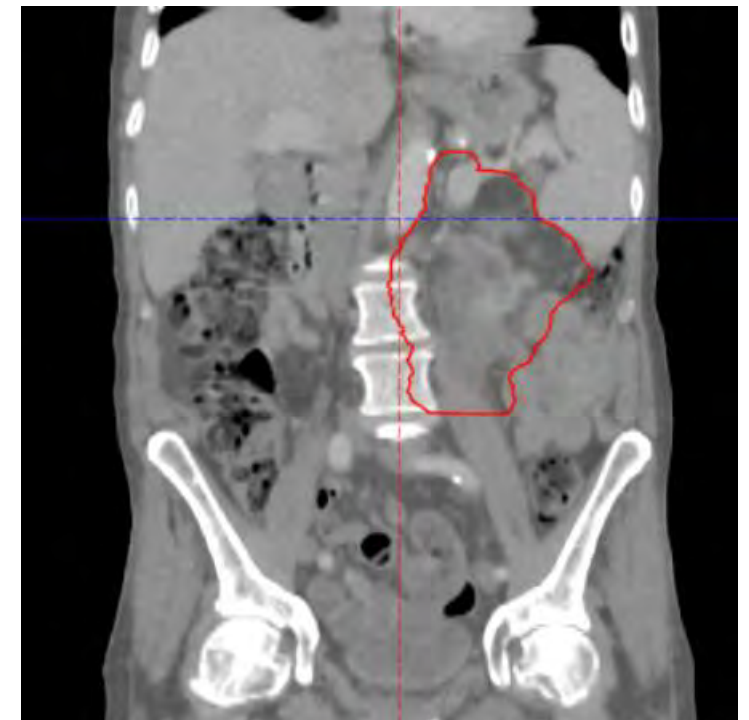
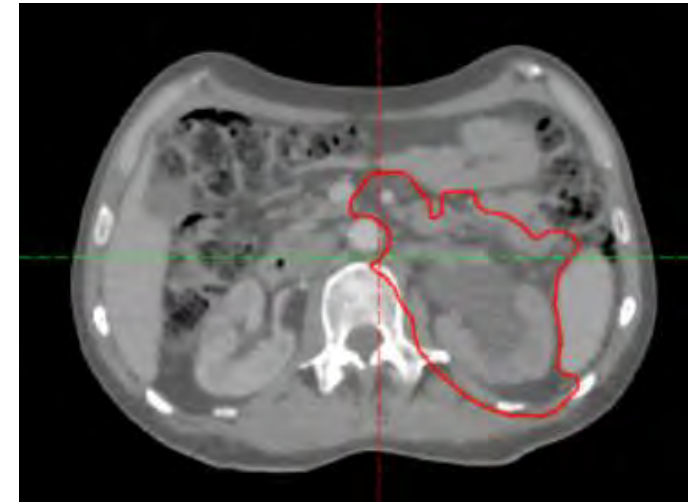
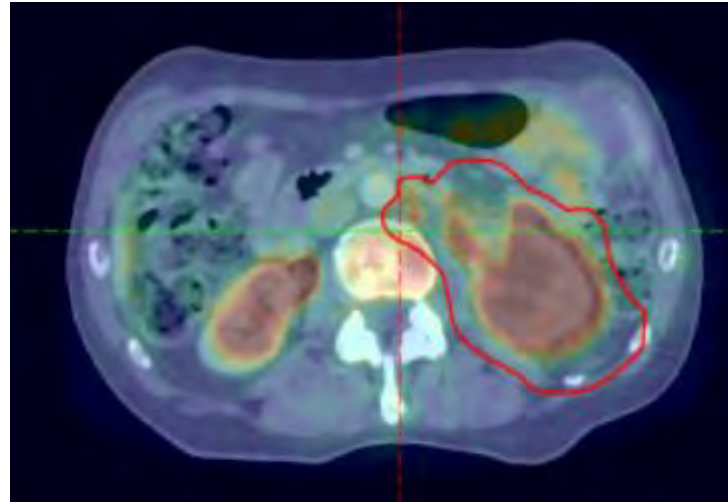


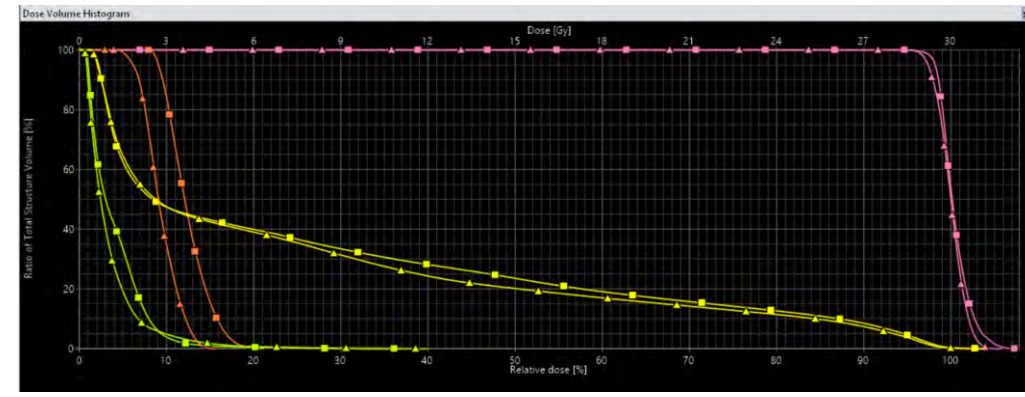
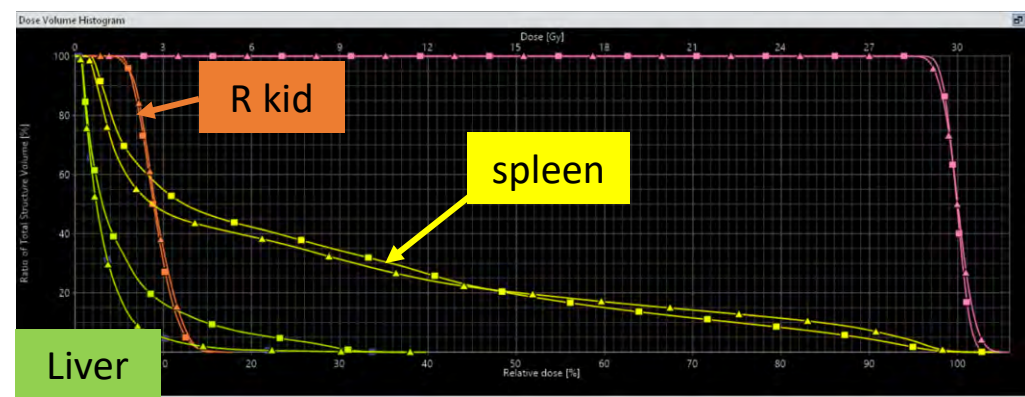
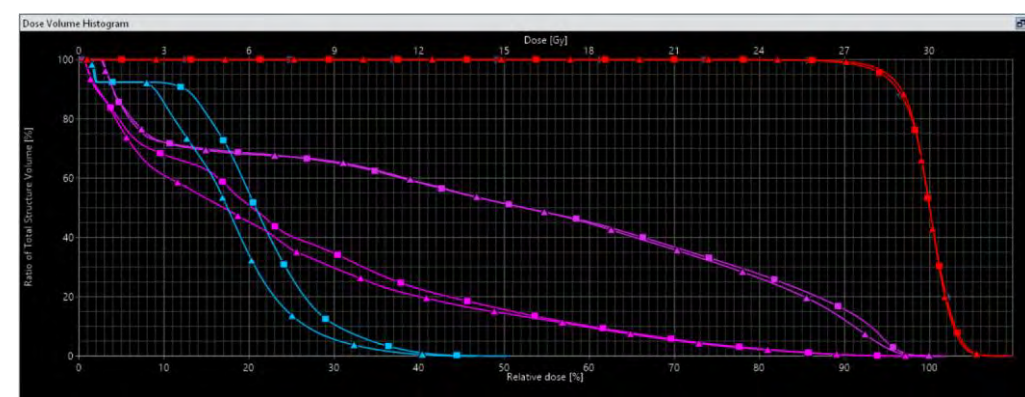
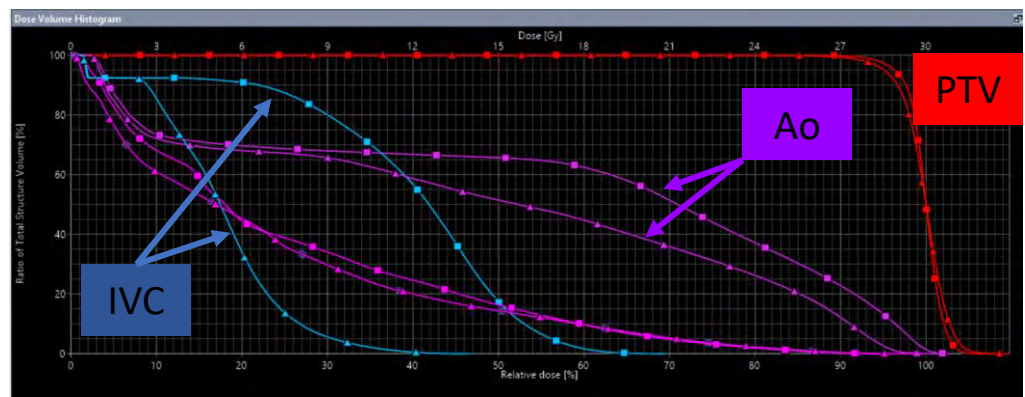
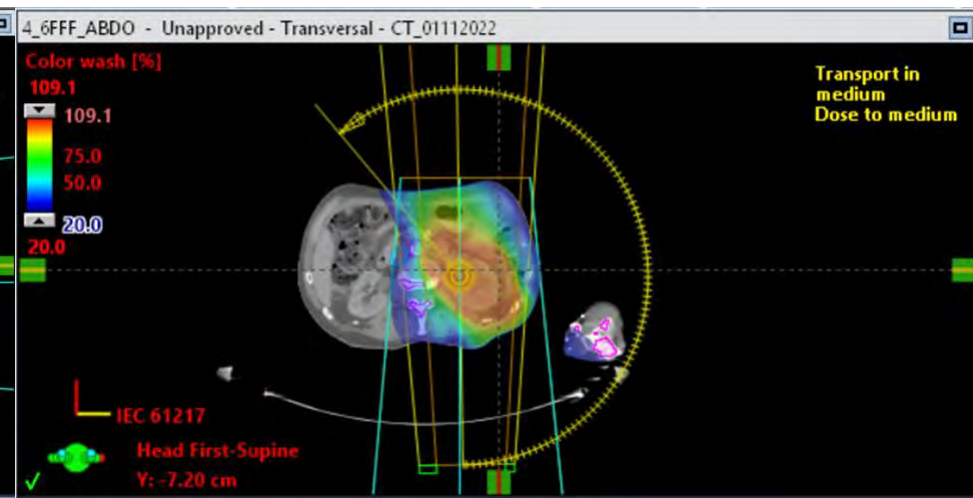
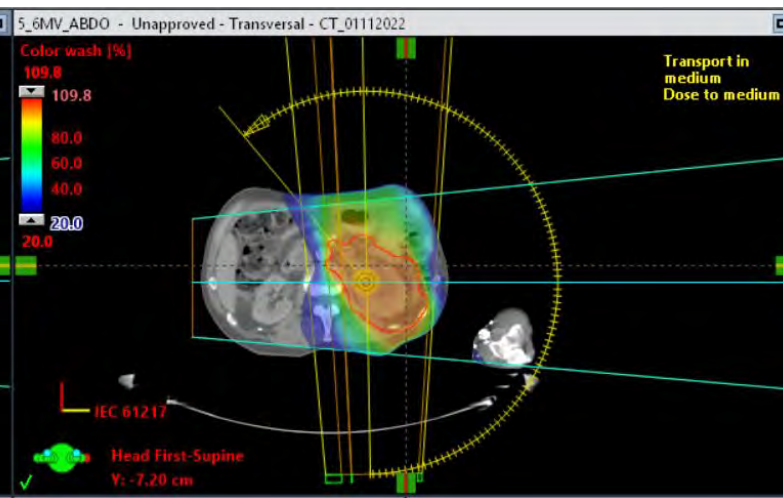
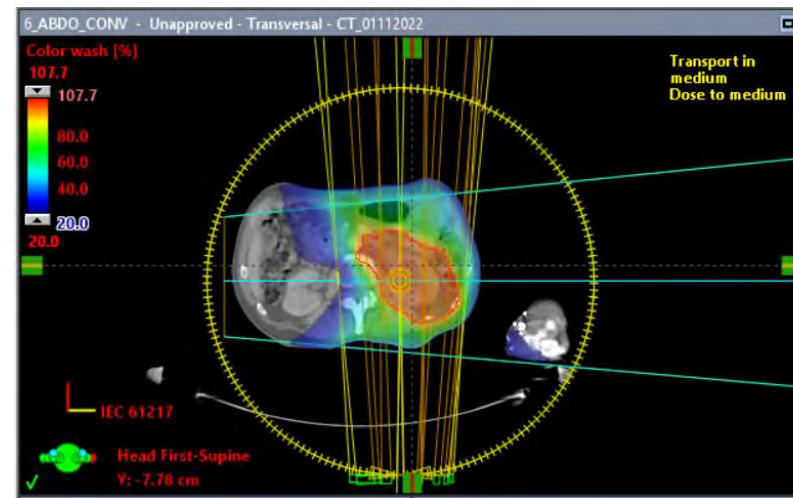
- Volume: residual / high risk lesion
- Dose: EQD2 = 30-40 Gy
- Technique: **CAR-T sparing**

78 male
R/R DLBCL DE
Stage 4

RCHOPx6 + MTX
Platinum-based salvage

Bridging R-Pola-Benda: DS-5
Tisa-cell





Conclusions

- RT before CAR-T can be used for several purposes:
 - Bridging
 - Debulking
 - Priming
- Purpose of RT varies according to timing and clinical case
- Choice of dose/fractionation, volume and technique:
 - Timing + purpose of RT
- Post-CAR-T RT: CAR-T-sparing RT techniques are under development

Thank you

Guy's and St Thomas' NHS Foundation Trust
Cancer Centre
at Guy's

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