ILROG
INTERNATIONAL LYMPHOMA RADIATION ONCOLOGY GROUP

4th ILROG Educational Conference:
Radiotherapy in Modern Management of Haematological Malignancies

RT with CAR-T: The Available Data

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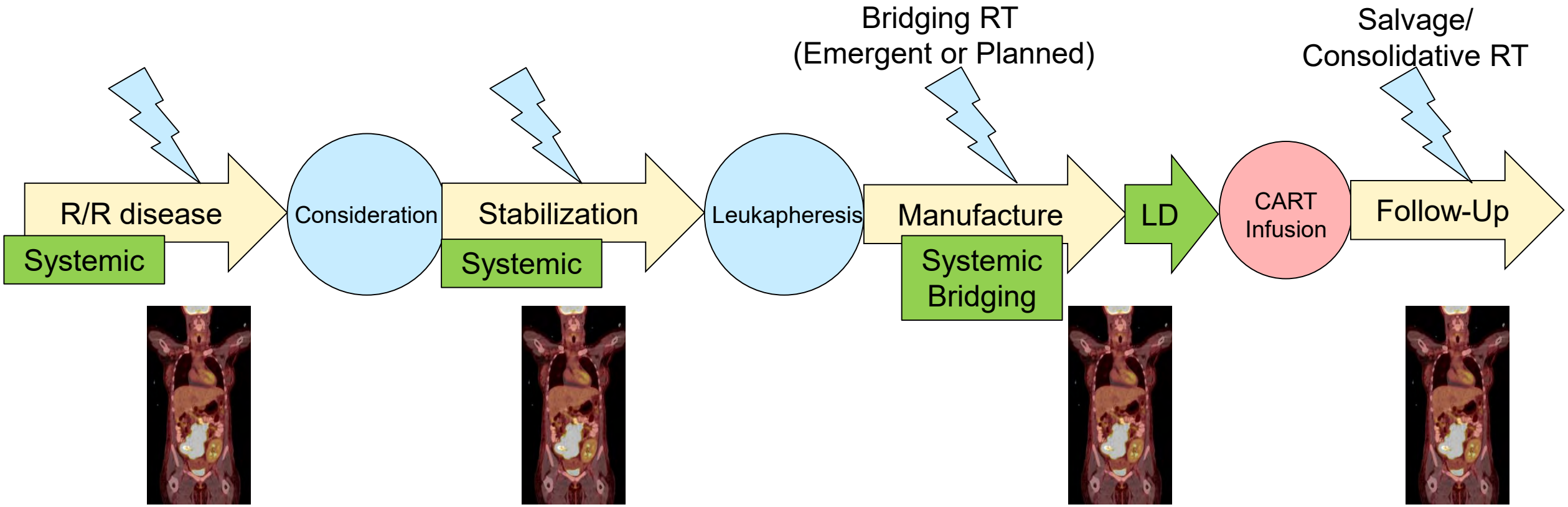
Disclosure

- Employer: University of Pennsylvania, Steering Committee of ILROG, IBA Proton Therapy advisory committee member
- Spouse: University of Pennsylvania, Member of ASTRO Board

- I have no conflicts of interest to disclose.

CART Workflow Timeline

- **Manufacture can take 3+ weeks, but many steps in process, including approvals**



Questions: Toxicity, Timing, Volume, Dose?

- Does RT cause **excess toxicities** that interfere with CART or exacerbate CRS/ICANS?
- Any impact of bridging RT on **outcomes** (PFS, OS)?
- What **timings** have been used with respect to apheresis, systemic bridging, lymphodepletion, CAR-T infusion?
  - How much time to recover from RT before LD chemotherapy?
  - Does RT play any role AFTER CAR T?
- What is the optimal bridging radiation **volume**?
  - Sub-portion of gross disease, aka “focal”?
  - All PET-avid disease, aka “comprehensive” RT?
- What RT **dose and fractionations** have been used?
- What is the role of **imaging** during, after bridging RT? After CART?

Summary of Single Institution Retrospective Studies

Study	Arscott et al	Sim et al	Imber et al	Qu et al	Wright et al	Pinnix et al	Saifi et al
CAR T product	tisa-cel	axi-cel	Multiple CAR T-cell products*	Investigational product targeting CD19, CD20, and CD22	tisa-cel, axi-cel	axi-cel	tisa-cel, axi-cel, brexu-cel
Number of patients who received bridging RT	5	12	11	6	5	11	14
Median RT dose in Gy (range)	N/A	20 (6–36.5)	20 (20–47)	40 (all the patients received the same dose)	37.5 (20–45)	35.2 (10–45)	20 (15–36)
Median RT fractions (range)	N/A	5.5 (3–14)	5 (5–26)	20 (all the patients received the same number of fractions)	15 (5–20)	N/A (the median fraction size was 2.5 Gy)	5 (3–24)
Sites of treatment	N/A	Abdomen, LLE/groin, hip, neck, chest wall	Neck, pelvis /groin, intra-abdominal, extremities	N/A	Retroperitoneum, mesenteric, nasal cavity, extremities	Spine, neck, thorax, abdomen/ pelvis	N/A
Median RT field size (range)	N/A	11.2 (3.7–29.4 cm)	887 (163–1641 cc)	N/A	445.5 (109–2077 cm^3)	N/A	N/A
OS%	100 (1 yr)	N/A	N/A	N/A	80 (1 yr)	63 (1 yr)	67 (1 yr)
PFS%	78 (1 yr)	N/A	N/A	N/A	20 (1 yr)	44 (1 yr)	47 (1 yr)
ORR%	N/A	81.8 (at 12-month follow-up)	60 (at day 90)	100 (after a median follow-up of 11 months)	80 (after a median follow-up of 12.3 months)	100	85.7
CRS-G3-5%	0	9	9	0	0	0	7
NT-G3-5%	N/A	18	27	0	0	27	21

- Abbreviations: RT, radiation therapy; OS, overall survival; PFS, progression-free survival; ORR, objective response rate; LLE, left lower extremity; CRS, cytokine release syndrome; NT, neurotoxicity.
* axi-cel, JCAR017, tisa-cel, EGFRt/19-28z/4-1BBL "armored" CAR-T.

Ababneh HS, Abramson JS, Johnson PC, Patel CG. Assessing the role of radiotherapy in patients with refractory or relapsed high-grade B-cell lymphomas treated with CAR T-cell therapy. Radiother Oncol. 2022 Oct;175:65-72.

Early Experience with Bridging: is it safe?

- Moffitt (2019): 11 pts had RT, then CART. No sig toxicity. ALC counts dipped (med, 0.25)
- MDACC (2020): 11/124 had bridging RT alone. 6/124 had combined modality bridging. 45/124 had systemic bridging. No diff in CRS/ICANs between combined bridging and non-bridging group.
- Upenn (2020): 5/31 had bridging RT. No Gr>/=3 RT-related toxicity.

Radiation Therapy as a Bridging Strategy for CAR T Cell Therapy With Axicabtagene Ciloleucel in Diffuse Large B-Cell Lymphoma

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REGULAR ARTICLE

blood advances

Bridging therapy prior to axicabtagene ciloleucel for relapsed/refractory large B-cell lymphoma

Chelsea C. Pinnix,[1] Jillian R. Gunther,[1] Bouthaina S. Dabaja,[1] Paolo Strati,[2] Penny Fang,[1] Misha C. Hawkins,[2] Sherry Adkins,[2] Jason Westin,[2] Sairah Ahmed,[2] Luis Fayad,[2] Hun Ju Lee,[2] Ranjit Nair,[2] Raphael E. Steiner,[2] Swaminathan P. Iyer,[2] M. Alma Rodriguez,[2] Michael Wang,[2] Christopher Flowers,[2] Sattva S. Neelapu,[2] and Loretta J. Nastoupil[2]

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Bridging Radiation Therapy Before Commercial Chimeric Antigen Receptor T-Cell Therapy for Relapsed or Refractory Aggressive B-Cell Lymphoma

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Can RT Debulking Decrease CART Toxicity?

- **Does bridging RT have comparable (*or decreased?)* rates of CART-related toxicities (CRS and ICANS) compared to non-bridging RT groups?**
  - Anecdotal evidence of decreased CART toxicity: Wright et al[1], Pinnix et al[2],Qu et al[3]

Author	Wright et al	Pinnix et al	Qu et al**
≥G3 CRS* Bridging RT, N(%)	0 (0)	0 (0)	0 (0)
≥G3 CRS* NBRT, N(%)	6 (23%)	10 (9%)	4 (100%)
≥G3 ICANS* Bridging RT, N (%)	0 (0)	3 (27%)	0 (0)
≥G3 ICANS* NBRT, N (%)	4 (15%)	43 (40%)	3 (75%)

*Differing CRS and ICANS grading scales across studies
** Enrolled 10 patients, 6 treated with bridging RT to 40Gy in 20 fx

1. Wright et al, IJROBP, 2020
2. Pinnix et al, Blood adv, 2020
3. Qu et al, J Immunotherapy, 2019

MULTICENTER COMMERCIAL CART REVIEWS

- UK experience
- US ILROG CART RT Consortium

Radiotherapy bridging in large B-cell lymphoma patients receiving CD19 CAR T – The UK experience

Andrea Kuhnl
King's College Hospital London
17-ICML meeting 2023

A Kuhnl, C Roddie, AA Kirkwood, S Chaganti, J Norman, S Lugthart, W Osborne, A Gibb, C Gonzalez Arias, A Latif, B Uttenthal, F Seymour, C Jones, D Springell, JL Brady, T Illidge, A Stevens, E Alexander, L Hawley, N O'Rourke, C Bedi, R Prestwich, J Frew, D Burns, M O'Reilly, R Sanderson, S Sivabalasingham, NG Mikhaeel

NHS

KING'S HEALTH PARTNERS

An Academic Health Sciences Centre for London

Pioneering better health for all

CAR T patients undergoing bridging therapy

CAR-T approved
N = 763

Between Dec 2018-Oct 2022 across 12 UK centres
N=583 axi-cel, N=180 tisa-cel

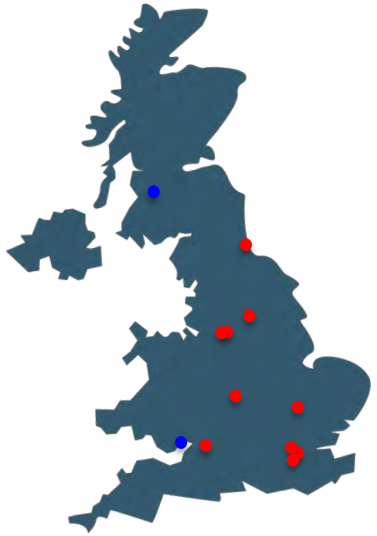
Not apheresed
N=41

Apheresis
N = 722

No bridging data
N=5

Bridging therapy
N = 644 (90%)

No bridging
N = 73 (10%)



RT bridging
N = 170 (24%)

Systemic
N = 435

Steroids only
N = 39

Single mod. RT
N = 129

CMT
N = 41

RT bridging use between centres:
11.1 – 32.4%

Increased use of RT over time:
19% (2018-19) to 26% (2021-22); p=0.034

CMT: combined modality treatment

Infusion rate 85.5%
No sign. difference between bridging modalities

RT details and toxicity

RT details	RT-SM	CMT
Technique; n=59		
IMRT	34	6
3D conformal	6	2
Simple	7	4
Dose; n=79; median (range)	30 Gy (2-39)	20 Gy (8-30)
Equivalent dose (EQD2); n=75; med (range)	30 Gy (1.83-42.3)	23.3 Gy (9.33-32.5)
Fractions, n=75; median (range)	10# (2-20)	5# (2-15)
RT toxicity, ≥G3; n=63	1*	0
CAR T toxicity; n=613		
≥G3 CRS	6 (5.1)	4 (11.8)
≥G3 ICANS	19 (16.2)	3 (8.8)

No difference between bridging modalities

*G3 vomiting (abdominal field), leading to early treatment termination after 22Gy (30Gy planned)

RT details and toxicity

RT details	
Technique; n	
IMRT	
3D conf	
Simple	
Dose; n=	
Equivaler	
Fractions, n-	
RT toxicity, ≥G3;	
CAR T toxicity; n=613	
≥G3 CRS	4 (11.8)
≥G3 ICANS	19 (16.2) 3 (8.8)

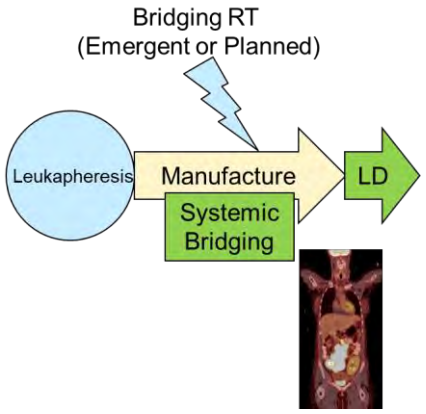
- ~1/4 get bridging RT
- ~2/3 treated with IMRT
- - emergent vs. planned
- No delay in CART delivery
- Most common dosing regimens:
  - 30 Gy/10 fx and 20 Gy/5 fx
- CART toxicities are within range of other studies

No difference between bridging modalities

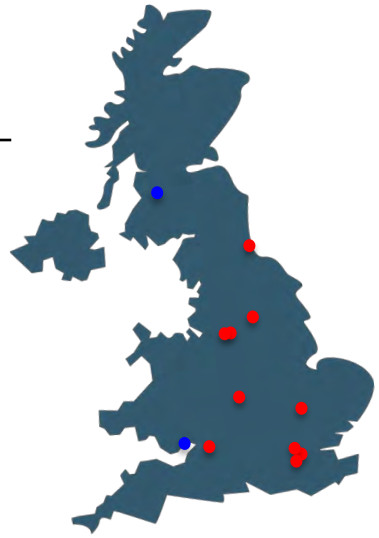
*G3 vomiting (abdominal field), leading to early treatment termination after 22Gy (30Gy planned)

Response to RT bridging

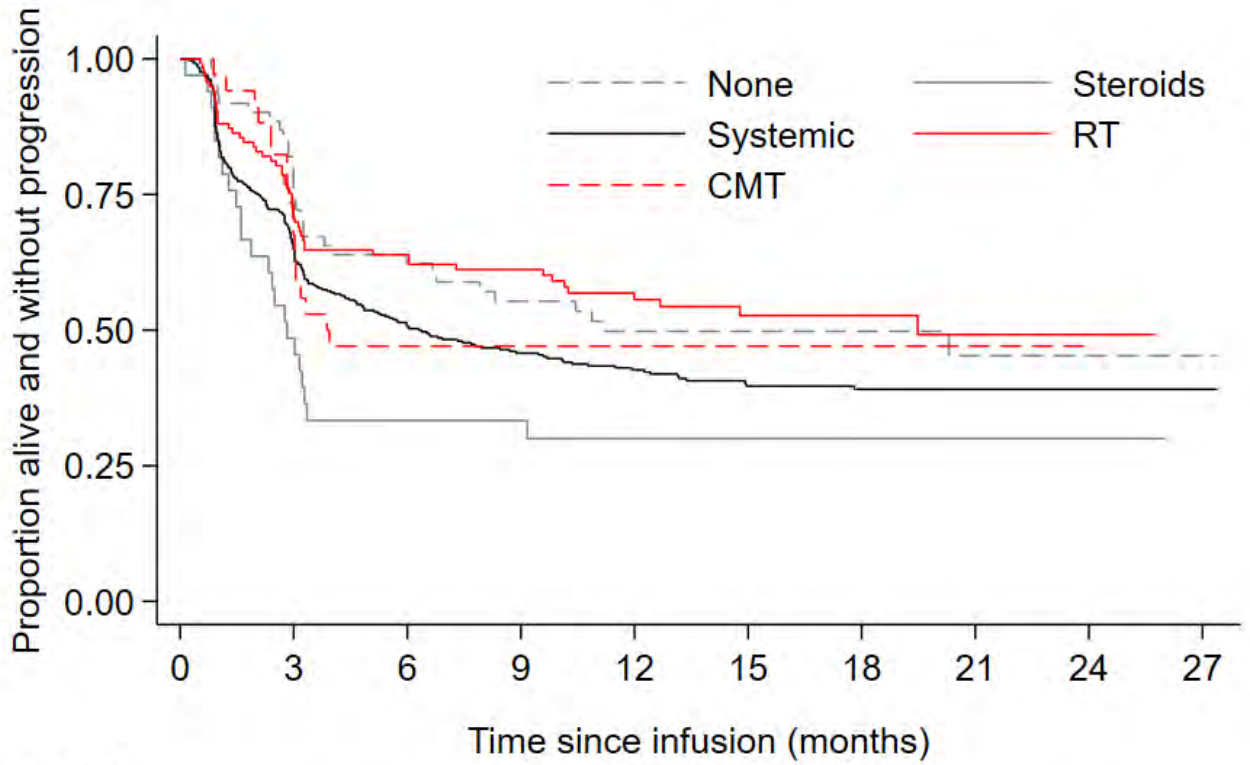
	All N (%)	RT-SM N (%)	CMT N (%)
In-field response			
CR	20 (17.2)	15 (16.5)	5 (20.0)
PR	79 (68.1)	64 (70.3)	15 (60.0)
SD	6 (5.2)	5 (5.5)	1 (4.0)
PD	11 (9.5)	7 (7.7)	4 (16.0)
Missing/Unknown	54	38	16
ORR	**99 (85.3)**	**79 (86.8)**	**20 (80.0%)**



Response based on pre-lymphodepletion PET scan= ~2 weeks after end of RT!



Progression-free survival



Number at risk

None	61	46	38	30	25	23	18	7	3	1
Steroids	33	16	11	10	9	8	8	6	1	0
Systemic	368	237	182	141	114	80	64	43	12	2
RT	117	82	72	61	44	31	18	10	4	0
CMT	34	23	14	10	10	8	4	3	1	0

	Med PFS (IQR)	1-year PFS (95% CI)
No bridging	11.1 (3.0 – NR)	49.8% (36.5 – 61.7)
Steroids	2.8 (1.5 – NR)	30.0% (15.5 – 45.9)
Systemic	6.3 (2.0 – NR)	42.7% (37.5 – 47.8)
RT (single mod)	19.5 (3.0 – NR)	55.6% (45.8 – 64.4)
CMT	3.9 (2.9 – NR)	47.1% (29.8 – 62.5)

Median follow-up 16 months

Abstract 191: Bridging Radiotherapy Prior to Chimeric Antigen Receptor (CAR) T-Cell Therapy for B-Cell Lymphomas: An ILROG Multi-Institutional Study

N. Yegya-Raman[1], C. M. Wright[1], C. J. Ladbury[2], J. Chew[3], S. Zhang[4], S. Y. Sun[5], S. Burke[6], J. Baron[1], A. J. Sim[7,8], M. J. LaRiviere[1], J. C. Yang[9], T. J. Robinson[7], Y. D. Tseng[10], S. A. Terezakis[5], S. E. Braunstein[3], S. V. Dandapani[2], S. Schuster[11], E. A. Chong[11], J. P. Plastaras[1], and N. B. Figura[7]

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Methods

- **Retrospective review of 115 patients with r/r BCL who received bridging RT prior to commercial CAR T**
- **2018 to 2020**
- **6 US academic institutions (will plan for 10 in our final analysis)**
- **Endpoints**
  - Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity (ICANS)
    - Per ASTCT and ASTCT/CTCAE v5.0
  - Best overall response (ORR) rate at 3 months
  - Patterns of failure
  - Progression-free survival (PFS) and overall survival (OS) from CAR T infusion

Timing, Volume, Dose, Fractionation: 6 US centers

Bridging Radiotherapy Characteristic	N (%) or Median (IQR)
By patient (N=115)	
Interval from leukapheresis to bridging RT start (d)	5 (-6-11)
Interval from bridging RT end to CAR T infusion (d)	14 (9-23)
Comprehensive bridging RT (to all lesions)	40 (35)
Nodal/Extranodal	
Nodal	43 (37)
Extranodal	48 (42)
Mixed	23 (20)
Unknown	1 (1)
Max diameter of largest treated lesion (cm)[1]	6 (3.6-10.2)
Concurrent systemic therapy	31 (27)
RT Technique	
3DCRT	52 (45)
IMRT	38 (33)
3DCRT/IMRT mix	5 (4)
Other/Unknown	20 (17)
Number of sites treated with RT	
1	85 (74)
2	17 (15)
3	8 (7)
4	5 (4)

Bridging Radiotherapy Characteristic	N (%) or Median (IQR)
By RT site (N=163)	
Sites treated	
Abdomen/pelvis	58 (50)
Head/neck	34 (30)
Thorax	20 (17)
Extremity/soft tissue	20 (17)
Central nervous system[2]	13 (11)
Focal brain	7
Whole brain	2
Optic nerve	3
Leptomeningeal disease	1
Spine/paraspinal	10 (9)
Axilla	8 (7)
Biologically effective dose (alpha/beta=10)[3]	31.3 (24-39)
Most common regimens[3]	
30 Gy / 10 fractions	27 (17)
20 Gy / 5 fractions	22 (14)
20 Gy / 10 fractions	8 (5)
37.5 Gy / 15 fractions	8 (5)

[1] Unavailable for 12 patients
[2] 13 sites treated among 8 patients
[3] Excluding 1 patient with missing dose/fractionation details

Timing, Volume, Dose, Fractionation: 6 US centers

Bridging Radiothera		N (%) or odian (IQR)
By patient		
Inter (d		
2		
3		
4		

se/fractionation details

Timing:
-RT started usually started within a week of leukapheresis (med 6 d): **1/3 IMRT**
-median RT to CART was 2 weeks

Volume:
-35% treated with comprehensive
- 74% treated only 1 site

Dose/Fraction:
- Median BED 31.3
- 1/3 treated with classic palliative regimens
  - (30Gy/10 or 20Gy/5)
- Otherwise quite variable!

The US is not yet consistent with dose and fractionation

- **44 different dose and fractionation regimens were given to 162 unique sites**

Priming?

400cGy in 2Fx	1600cGy in 4Fx	2500cGy in 10Fx	3200cGy in 20Fx
800cGy in 1Fx	1750cGy in 7Fx	2500cGy in 5Fx	3240cGy in 18Fx
900cGy in 3Fx	2000cGy in 10Fx	2700cGy in 9Fx	3500cGy in 14Fx
1200cGy in 2Fx	2000cGy in 15Fx	2800cGy in 14Fx	3600cGy in 12Fx
1200cGy in 3Fx	2000cGy in 5Fx	2960cGy in 16Fx	3600cGy in 18Fx
1200cGy in 6Fx	2000cGy in 7Fx	3000cGy in 10Fx	3600cGy in 20Fx
1250cGy in 5Fx	2100cGy in 10Fx	3000cGy in 15Fx	3750cGy in 15Fx
1400cGy in 10Fx	2340cGy in 13Fx	3000cGy in 5Fx	3780cGy in 21Fx
1400cGy in 7Fx	2400cGy in 12Fx	3000cGy in 6Fx	4000cGy in 20Fx
1500cGy in 1Fx	2400cGy in 8Fx	3060cGy in 17Fx	4250cGy in 17Fx
1500cGy in 5Fx	2475cGy in 11Fx	3200cGy in 16Fx	4300cGy in 16Fx

Results: Safe, effective in field, especially comprehensive

- **Toxicity (~70% were treated with axi-cel)**
  - G3-4 CRS: 8%
  - G3-4 ICANS: 20%
  - No G3+ toxicities attributed to bridging RT
- **Patterns of failure**
  - Majority of failures at new lesions and out of bridging RT fields
- **Which factors predicted for better/worse PFS?**
  - Worse: Age, worse PS, CNS involvement, elevated LDH, high MTV (or TLG)
  - Better: Comprehensive bridging RT and use of Axi-cel
  - “Positive effect” of Comprehensive bridging RT appears to be independent of MTV

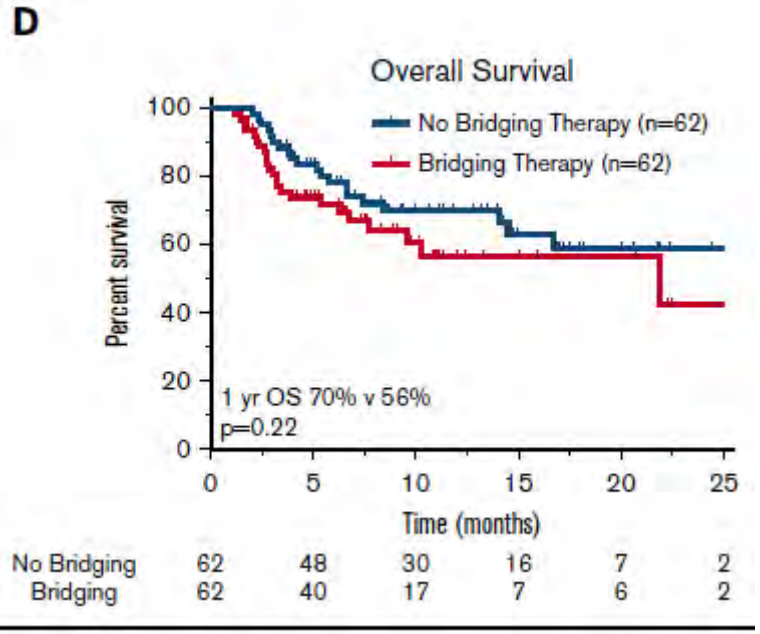
Comprehensive or Focal RT?

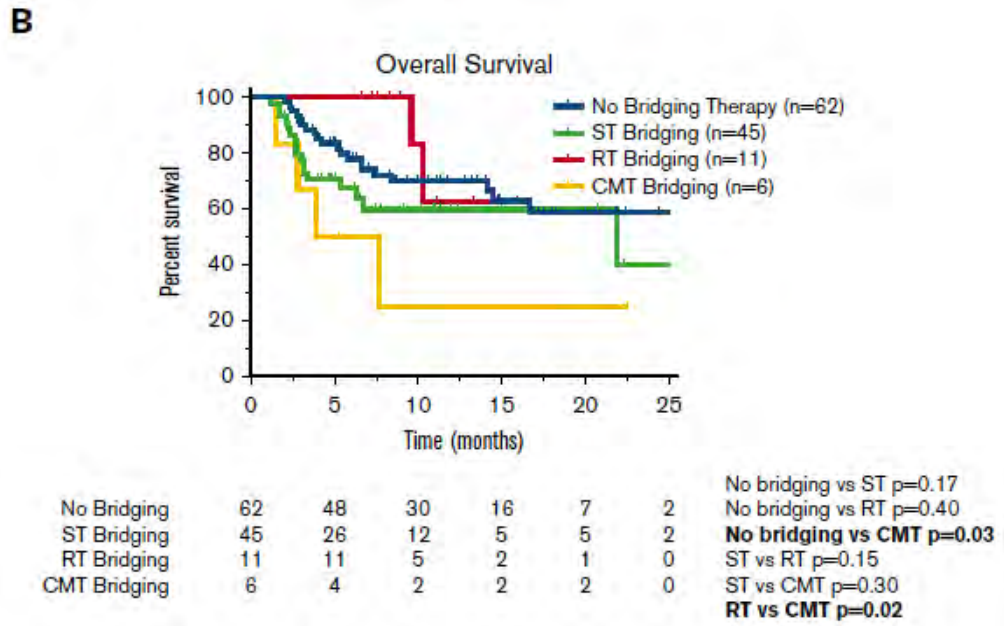
blood advances

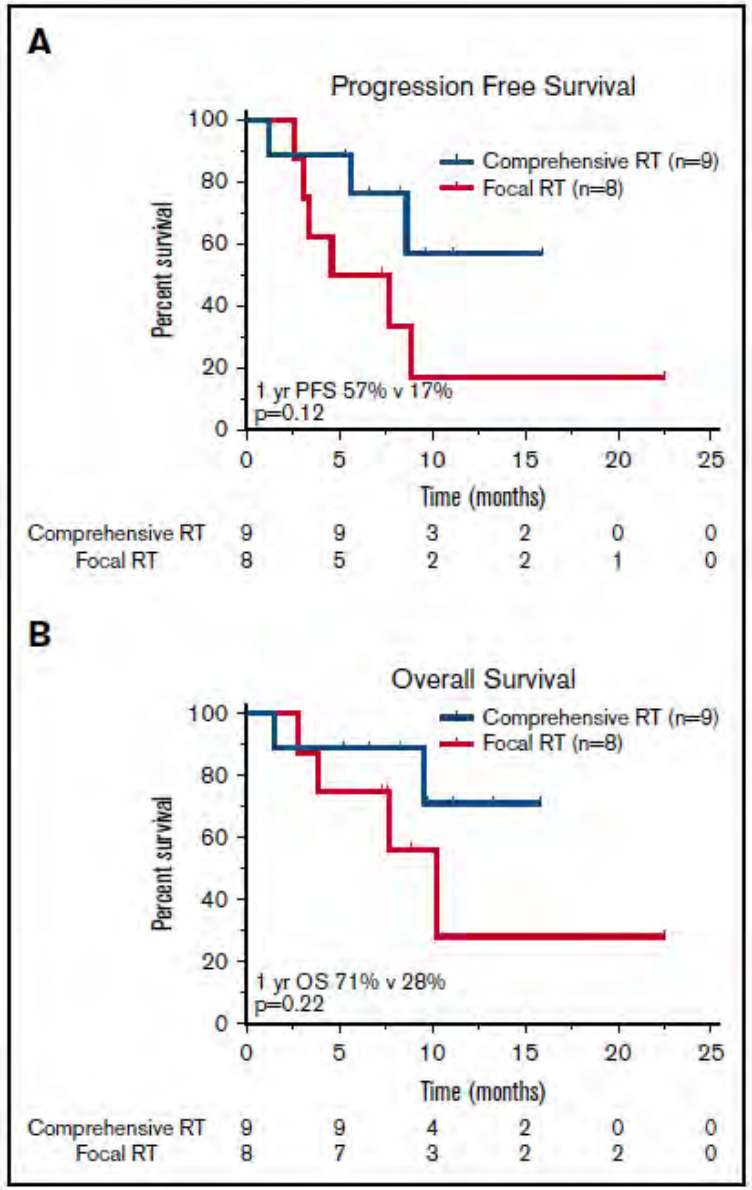
Bridging therapy prior to axicabtagene ciloleucel for relapsed/refractory large B-cell lymphoma

Pinnix et al. 2020 4(13): 2871

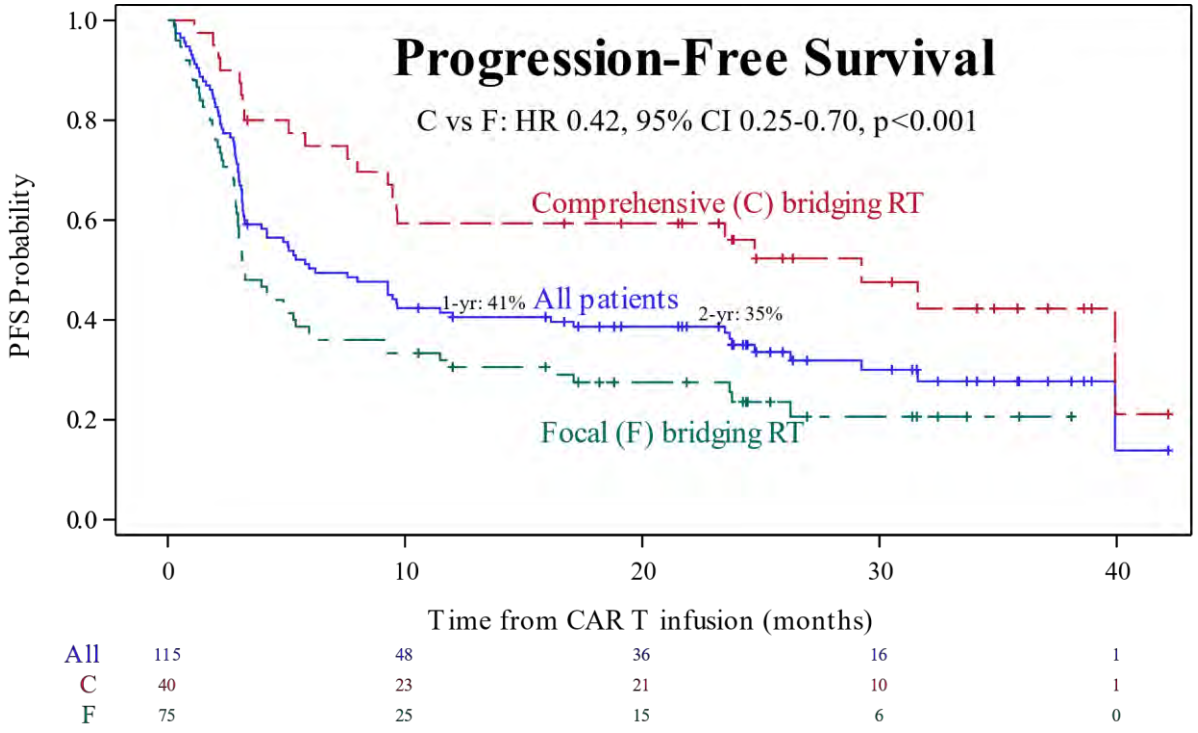
- **Any bridging associated with worse outcomes, but RT bridging seems a bit better than systemic**
- **Comp better than focal?**

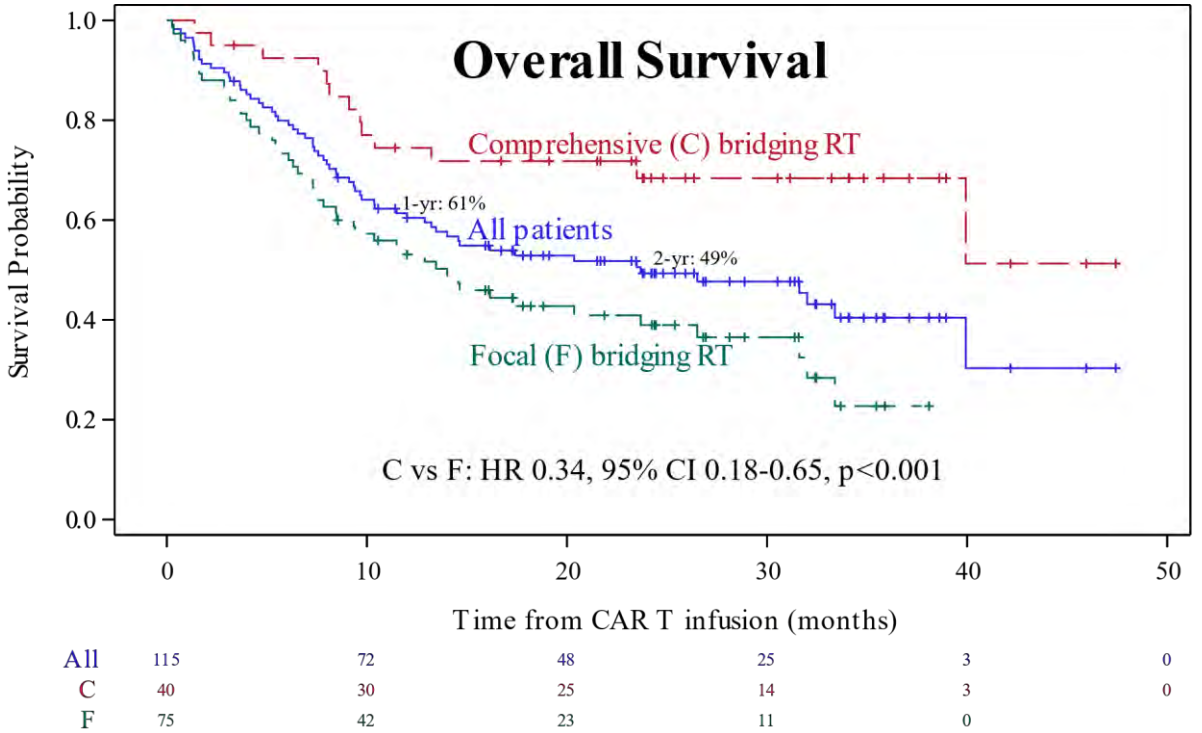






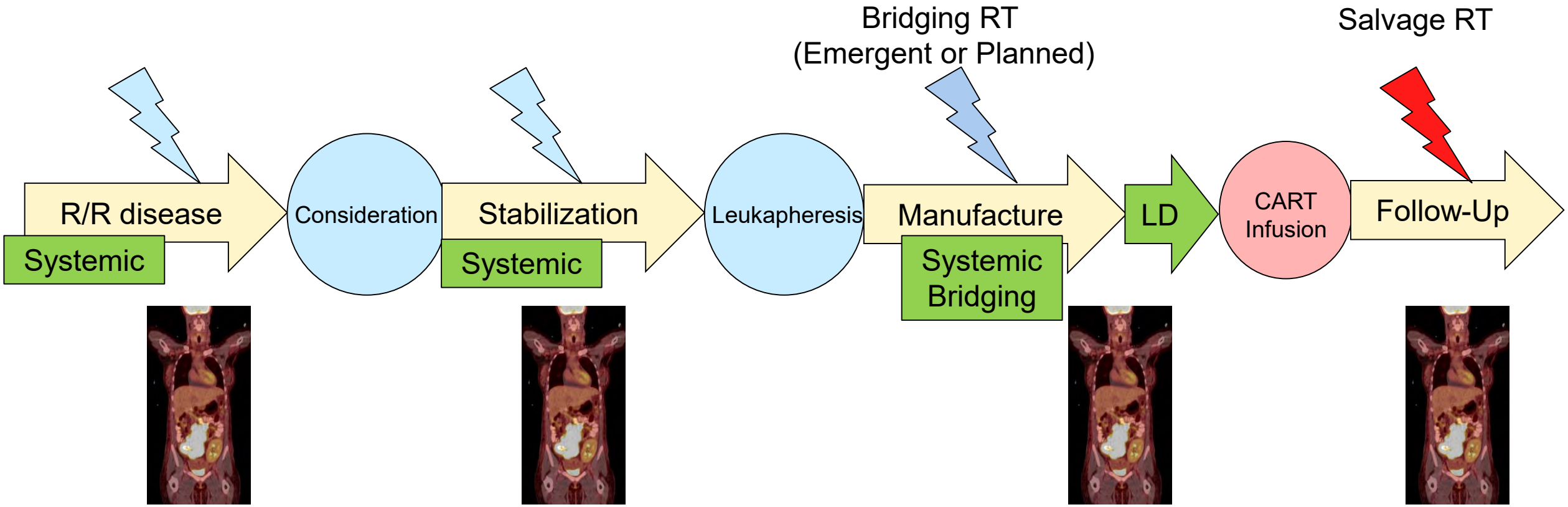
Comprehensive Bridging Associated with Better PFS/OS





CART Timing: Role of RT AFTER CART infusion?

- **Manufacture can take 3+ weeks, but many steps in process, including approvals**



Post-CART relapse: Salvage RT?

- **Rationale for salvage RT**
  - Effective for chemo refractory disease
  - Indirect immunomodulation?
    - Re-invigorating stalled CART responses?
  - Majority have local failure component when bridging RT is not used. **Bulk** and **SUVmax** are predictive of local failiure.

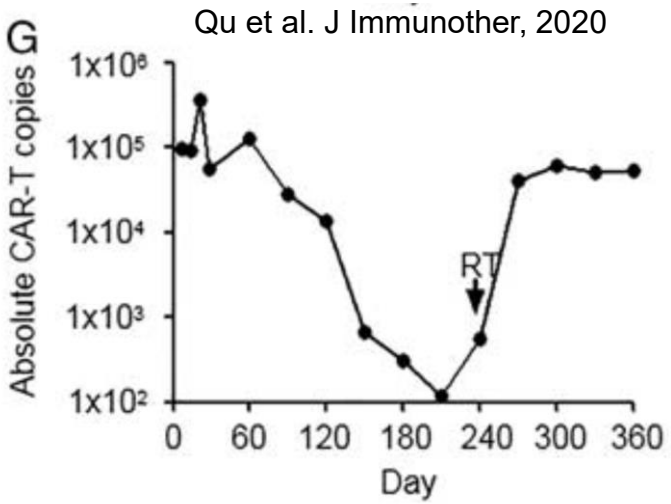
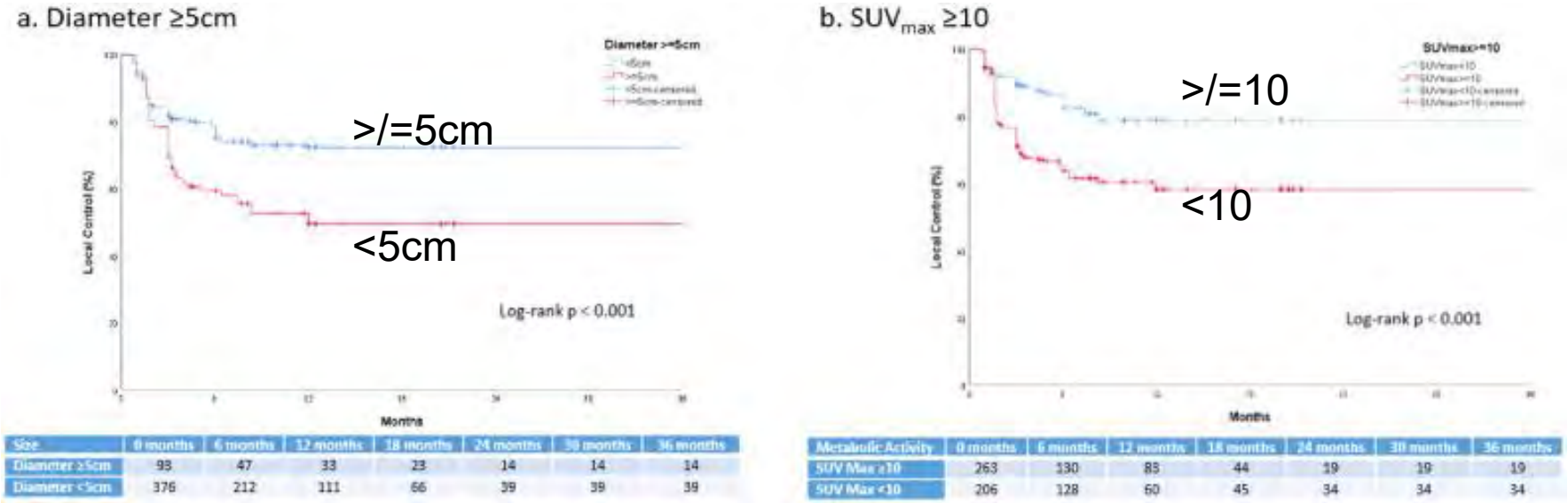


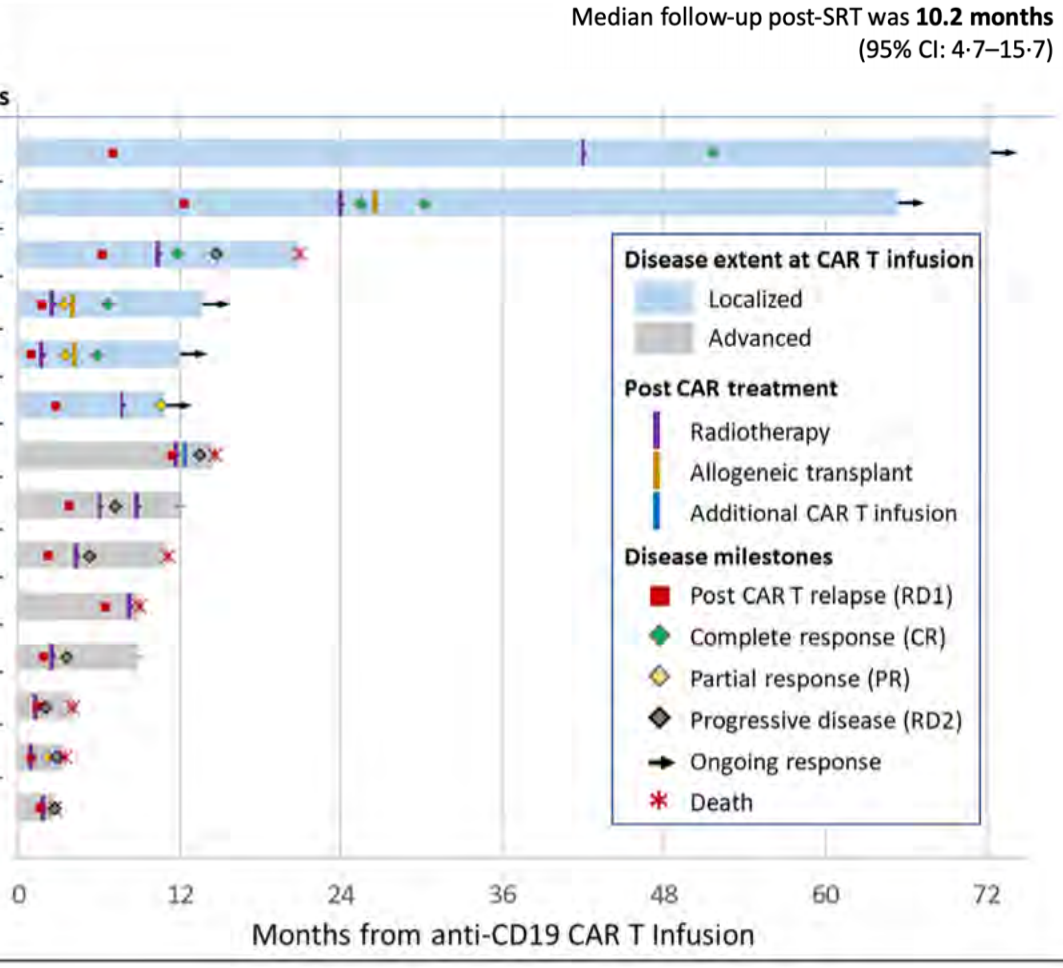
Figura et al. IJROBP 2021



Salvage RT – MSKCC experience

(A)

	CAR T product	Best post CAR T response	Indication for SRT	Irradiated site	SRT Dose (Gy)	SRT fractions
14	CAR 19-28z	CR	Focal relapse, follicular histology	Upper mediastinum	46	23
13	CAR 19-28z	CR	Bridge to alloSCT	Chest wall	36	18
12	JCAR017	PR	Focal relapse, chemorefractory	Mesentery	30	20
11	JCAR017	PR	Bridge to alloSCT	Mediastinum, manubrium	45	26
10	Tisa-cel	PD	Bridge to alloSCT	Mesentery	45	30
9	Tisa-cel	CR	Focal relapse, palliation	Thoracic paraspinal	20	5
8	JCAR017	PR	Augment CAR response	Mesentery/perinephric	20	5
7	Tisa-cel	CR	Palliation of neuro symptoms	WBRT	30	10
6	JCAR017	PR	Palliation, airway compromise	Larynx	30	10
5	"Armored"	CR	Palliation	Gluteal soft tissue	20	5
4	JCAR017	PR	Dominant site of progression	Mesentery	36	20
3	Axi-cel	PD	Palliation of cord compression	Thoracolumbar spine	20	5
2	JCAR017	PD	Palliation, airway compromise	Bilateral neck	20	10
1	JCAR017	PR	Palliation	Thigh cutaneous/soft tissue	30	15



In localized group, 3/6 were successfully bridged to alloHCT

Imber et al. BHJ, 2020

Salvage RT – Penn Experience

- **Retrospectively analyzed 21 patients who relapsed after CART therapy and subsequently received salvage RT from 05/2018 to 6/2020**

- **Post-CART relapse groups**
  - Locoregional disease (all relapsed disease encompassable within an RT field)
  - Advanced disease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Salvage radiotherapy for relapsed/refractory non-Hodgkin lymphoma following CD19 chimeric antigen receptor T-cell (CART) therapy

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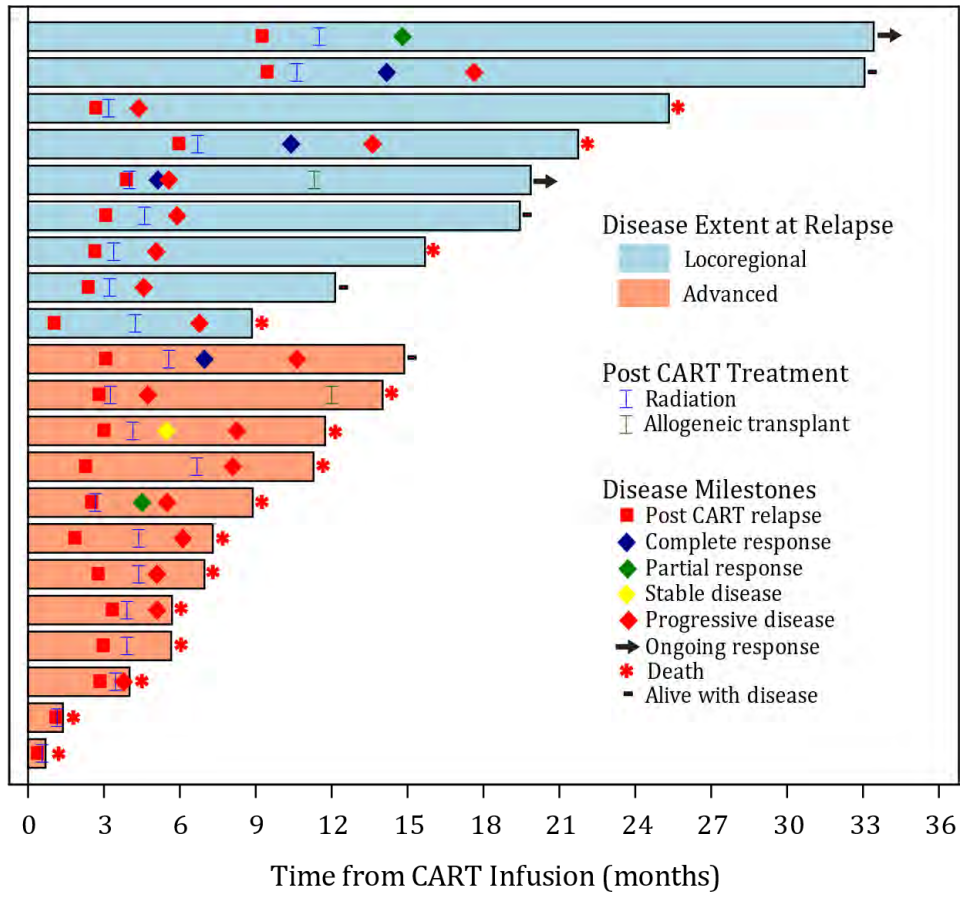
Salvage RT – Penn Experience

Patient	CART Product	Best Post CART Response	SRT Site	Comprehensive vs Focal (C vs F)	SRT Dose (Gy)	SRT Fractions
1	Tisa-cel	CR	Testicle	C	30.6	17
2	Tisa-cel	CR	Thigh soft tissue	C	37.5	15
3	Axi-cel	PD	Orbit	C	45	25
4	Tisa-cel	PR	Colonic mesentery	C	41.4	23
5	Tisa-cel	SD	Paraspinal masses	C	37.5	15
6	Axi-cel	PD	Adnexal masses	C	30.6	17
7	Tisa-cel	PD	Abdominal/pelvic wall masses	C	40.05	15
8	Tisa-cel	PD	Inguinal LN's	C	35	14
9	Tisa-cel	PD	Axillary LN	F	8	2
10	Tisa-cel	PD	Lung (hemoptysis)	F	12	4
11	Axi-cel	PD	Retroperitoneal LN	F	30	10
12	Tisa-cel	SD	T spine	F	20	5
13	Tisa-cel	PD	Duodenal mass	F	25	10
14	Tisa-cel	PD	Paraspinal mass	F	25	5
15	Tisa-cel	PD	Pelvic mass	F	27	9
16	Tisa-cel	PD	Thigh soft tissue	F	25	10
17	Axi-cel	PR	Paraspinal mass	F	20	5
18	Axi-cel	PR	Foot cutaneous	F	21.6	12
19	Tisa-cel	PD	Maxillary/pterygoid masses	F	20	5
20	Tisa-cel	PD	T spine (cord compression)	F	20	5
21	Tisa-cel	PD	T spine (cord compression)	F	8	1



- 18/21 with evaluable imaging post-SRT
  - **In field response: 16/18 (89%)**
  - **Distant relapse: 17/18 (94%)** → explains why most experienced PD after salvage RT
  - No isolated local or marginal relapses

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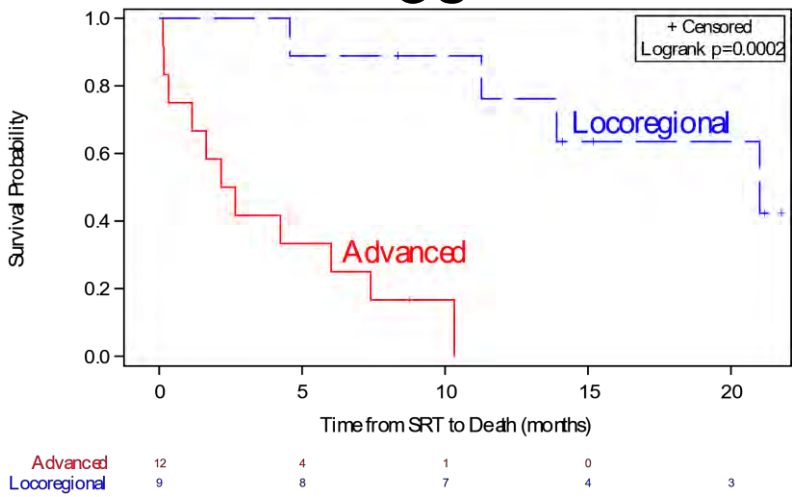
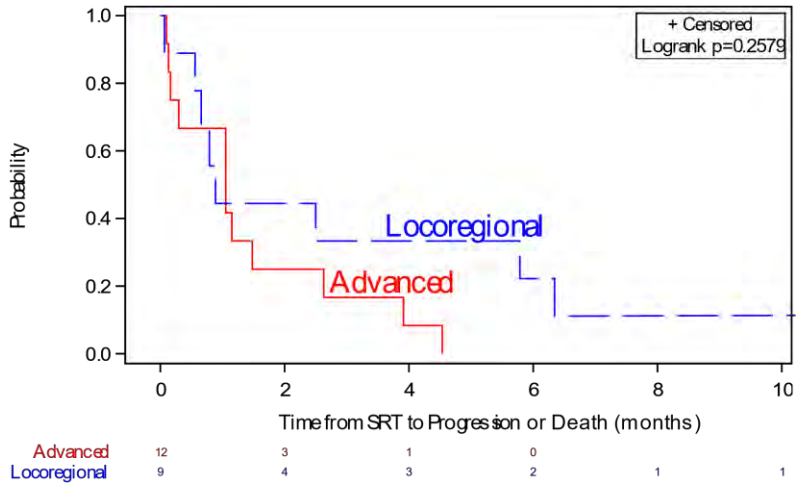
Outcomes after Salvage RT better with locoregional dz

- **OS better in locoregional group, but PFS poor regardless (due to distant progression)**

OS



PFS



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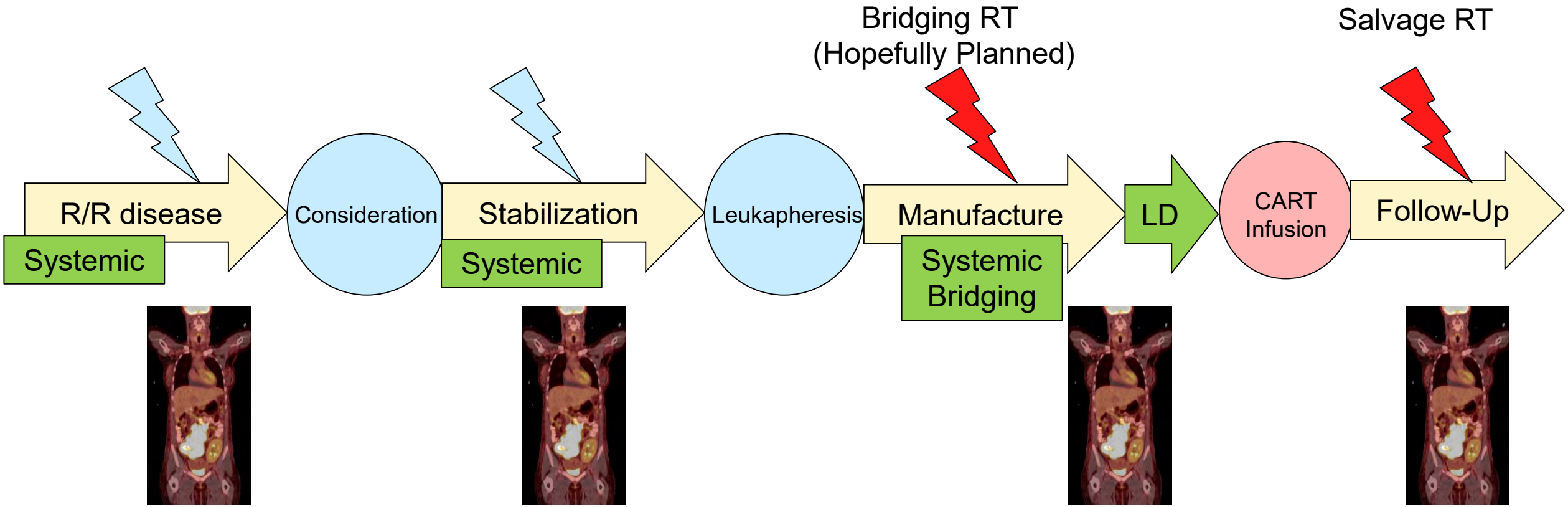
CART Workflow Timeline

- **Manufacture can take 3+ weeks, but many steps in process, including approvals**

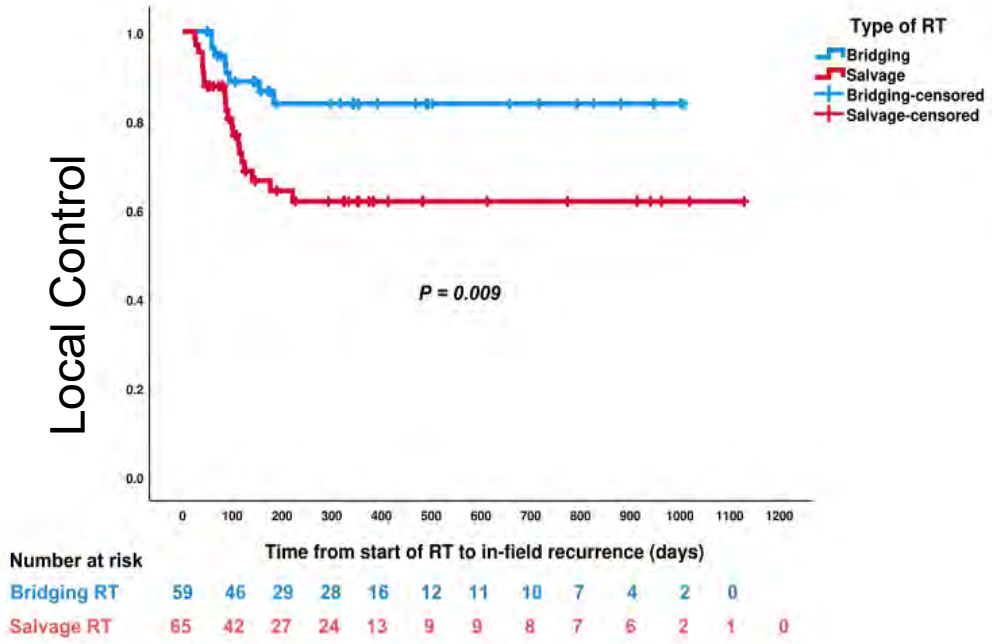


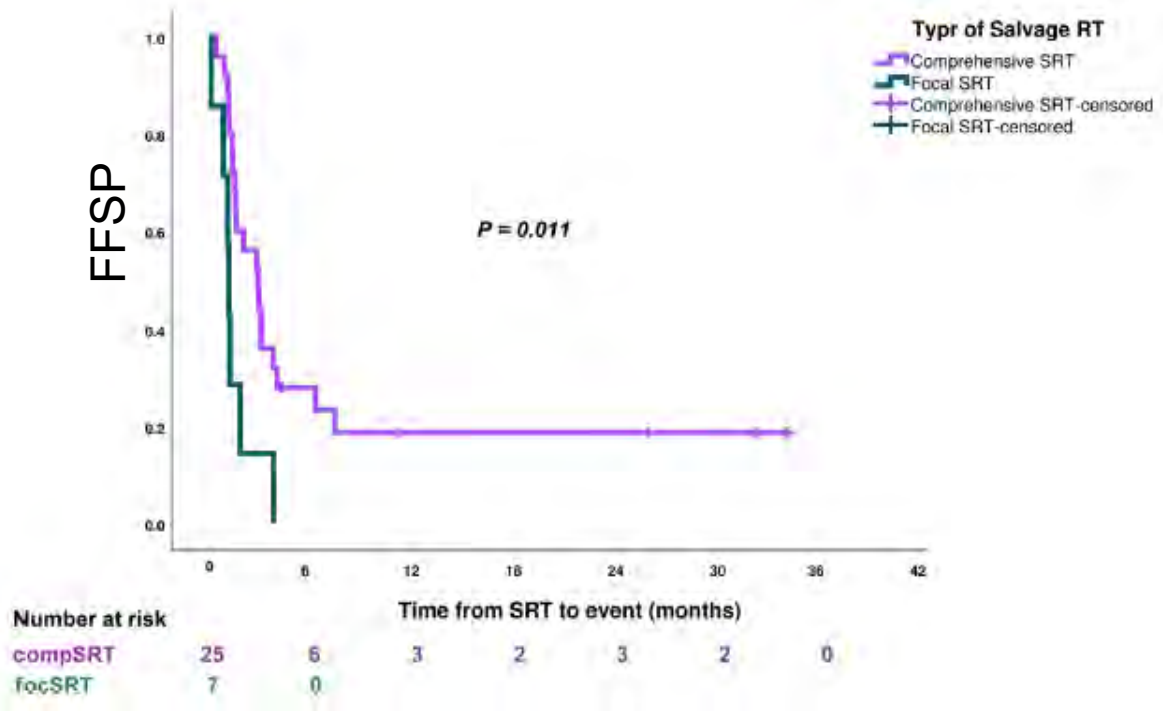
Timing: Bridging RT versus Salvage focal or comp RT

CLINICAL INVESTIGATION

Don't Put the CART Before the Horse: The Role of Radiation Therapy in Peri-CAR T-cell Therapy for Aggressive B-cell Non-Hodgkin Lymphoma

Omran Saifi, MD,* William G. Breen, MD,† Scott C. Lester, MD,† William G. Rule, MD,‡ Bradley J. Stish, MD,† Allison Rosenthal, DO,§ Javier Munoz, MD,§ Yi Lin, MD, PhD,‖,¶ Radhika Bansal, MBBS,‖ Matthew A. Hathcock,‖ N. Nora Bennani, MD,‖ Jonas Paludo, MD,‖ Arushi Khurana, MBBS,‖ Jose C. Villasboas, MD,‖ Patrick B. Johnston, MD, PhD,‖ Stephen M. Ansell, MD, PhD,‖ Madiha Iqbal, MD,# Muhamad Alhaj Moustafa, MD,# Hemant S. Murthy, MD,# Mohamed A. Kharfan-Dabaja, MD, MBA,# Bradford S. Hoppe, MD,* and Jennifer L. Peterson, MD*



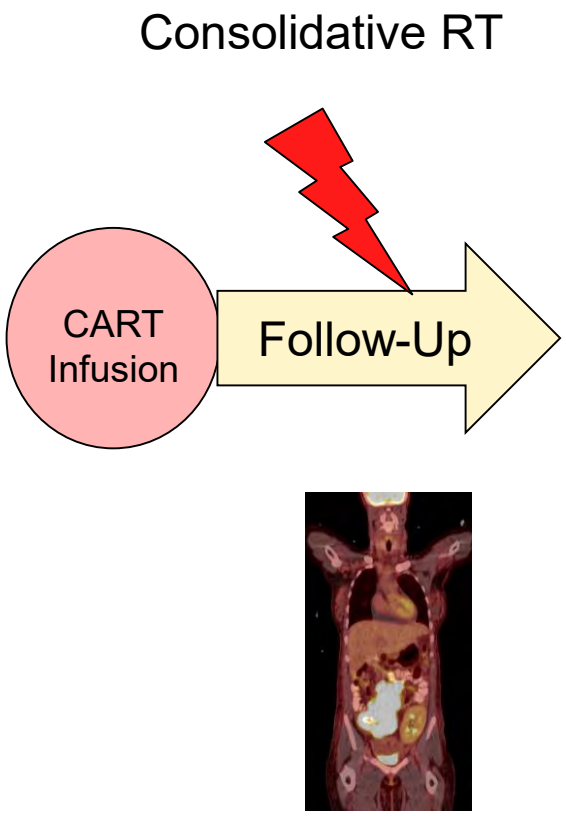


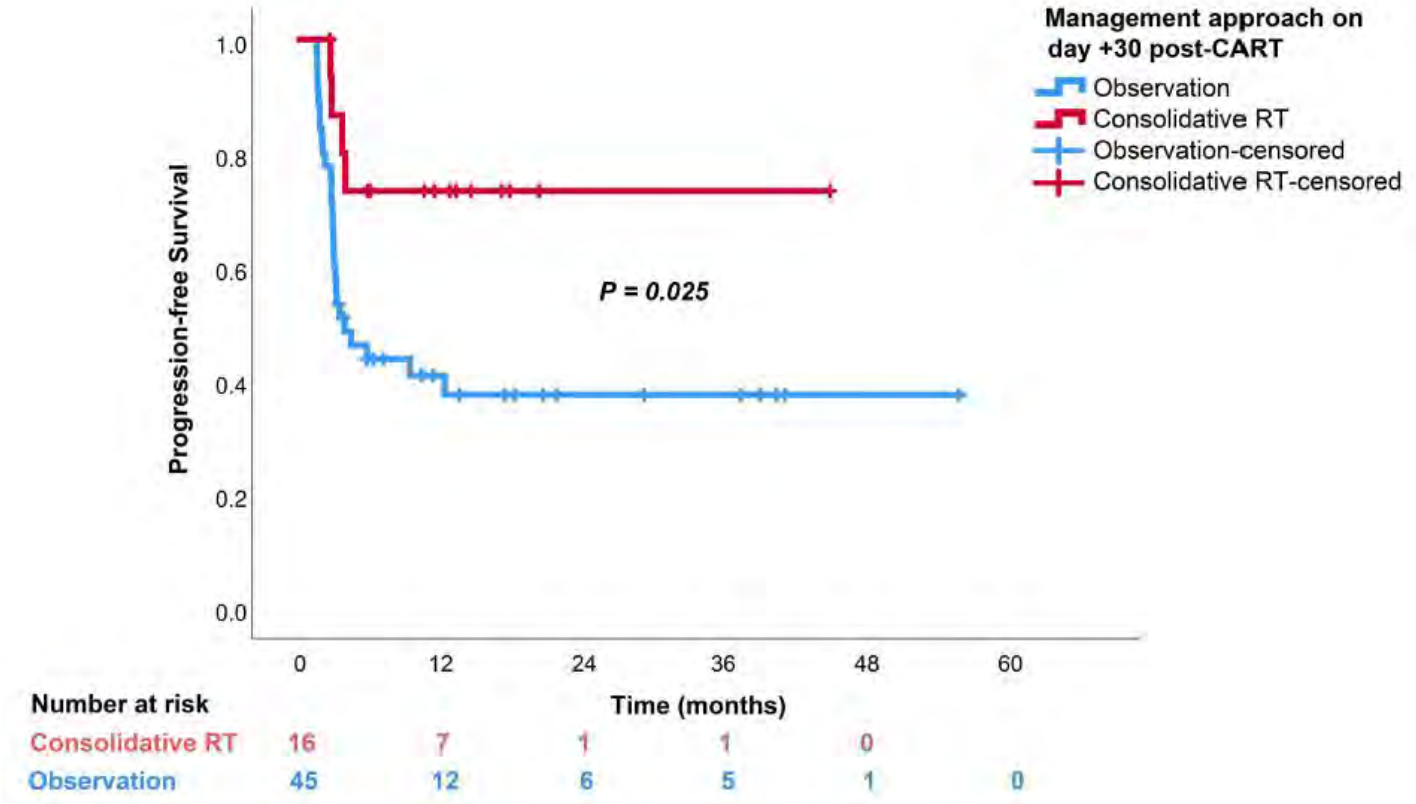
Pts with limited disease who received compSRT had significantly higher 1-year FFSP (failure from subsequent progression)

Saifi et al IJROBP 2023 Aug 1;116(5):999-1007

Consolidative RT for Incomplete CART Response?

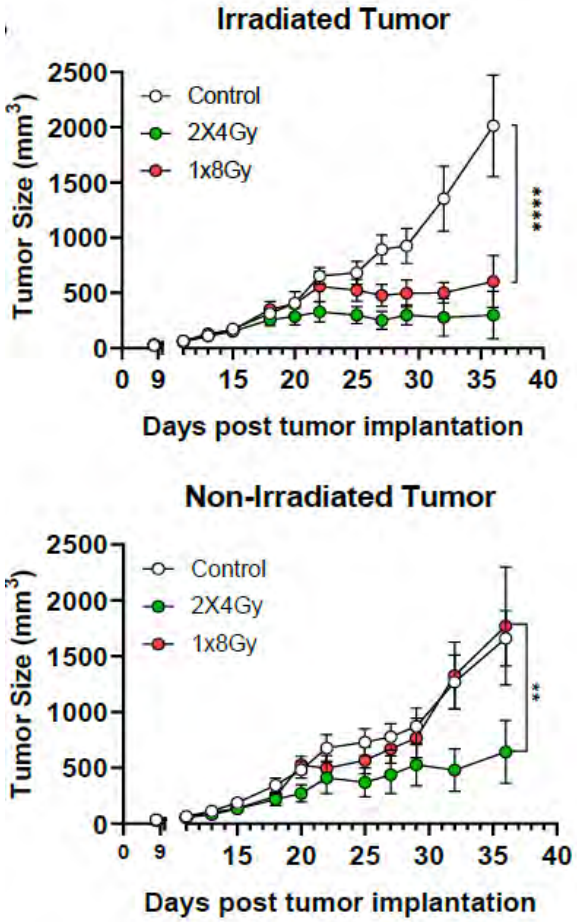
- N=61 who received CART with PR or SD on day+30 PET/CT
- 16/61 treated with consolidative RT

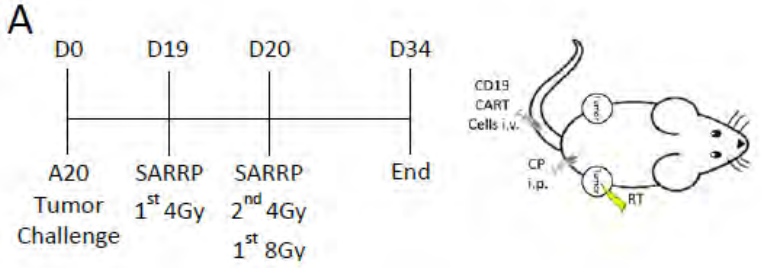




Saifi O et al. Haematologica. 2023 Jun 15

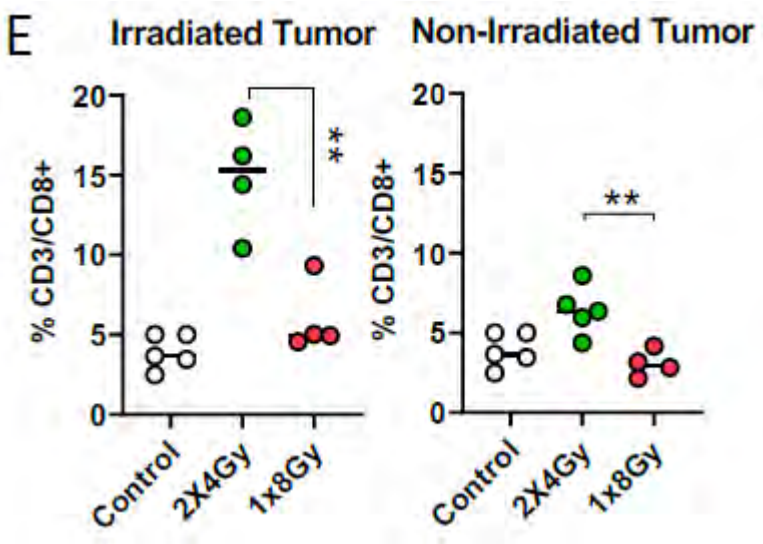
A20 mouse model of CD19+“DLBCL” – 4Gyx2 but not 8Gyx1 results in an abscopal effect





Nektarios Kostopoulos
Andrea Facciabene

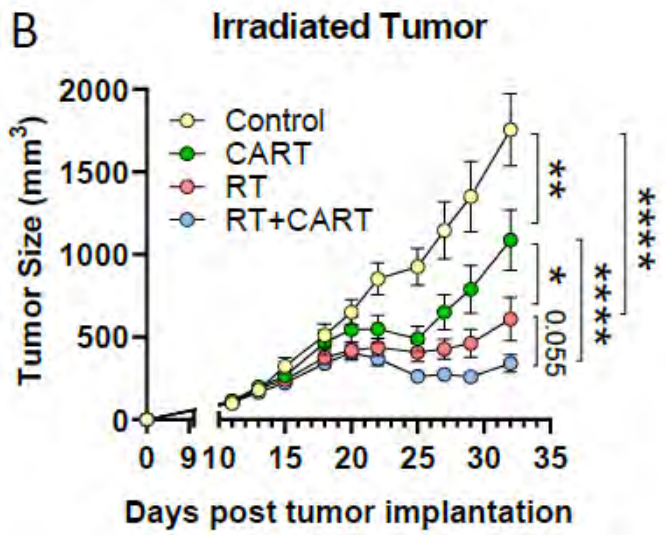
CD3+ infiltration enhanced by 2 fx

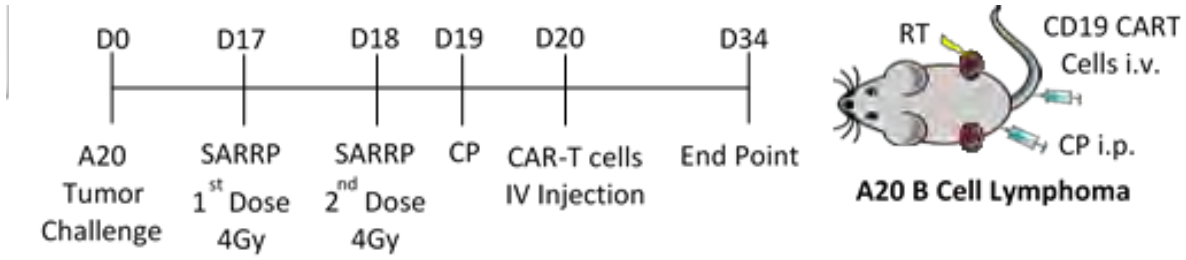


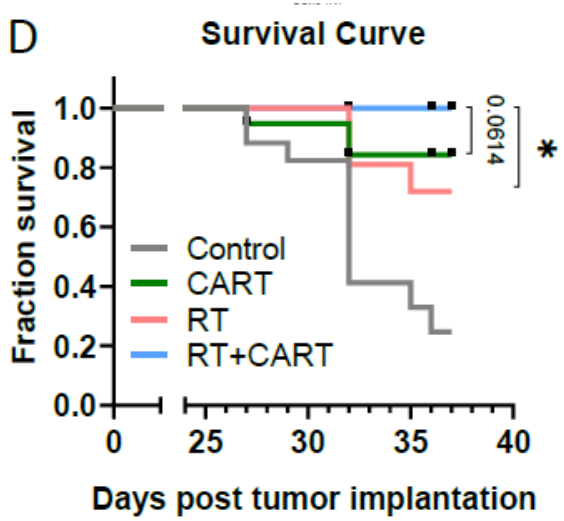
This A20 model has a baseline abcsopal effect with radiation alone (and other agents)
Considered a “hot” tumor

Kostopoulos N et al. AACR abstract 3449. 2022

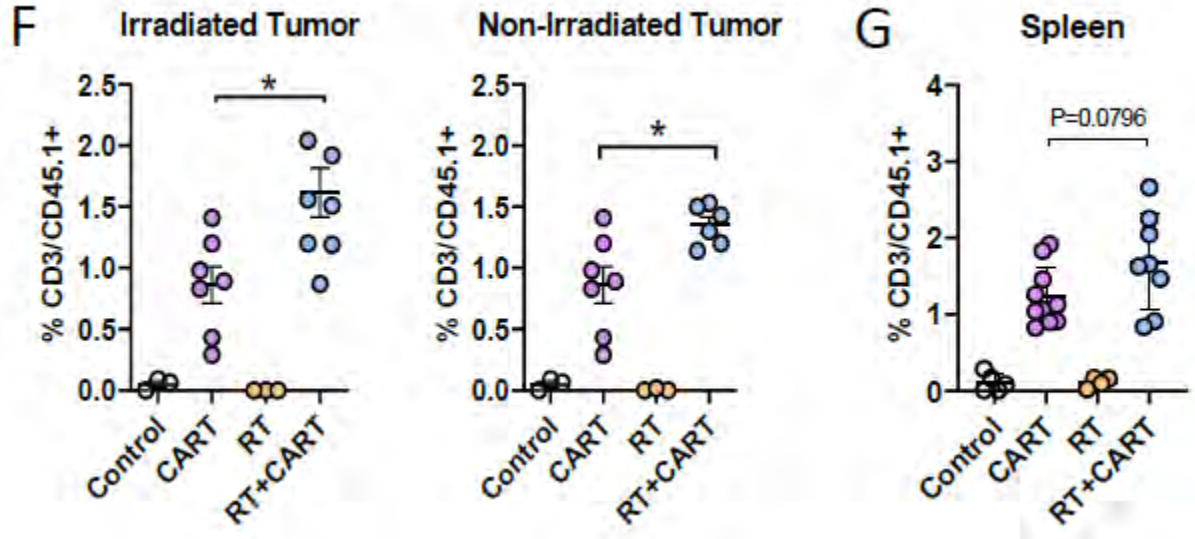
Bridging RT prior to CAR T improves the anti-tumor effect in both radiated and non-irradiated tumors







4Gyx2 increases CART cell trafficking to radiated, non-irradiated tumors and the spleen



Kostopoulos N et al. AACR abstract 3449. 2022

CART-BCMA for Multiple Myeloma

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

The Safety of Bridging Radiation with Anti-BCMA CAR T-Cell Therapy for Multiple Myeloma

Shwetha H. Manjunath[1], Adam D. Cohen[2], Simon F. Lacey[3,4], Megan M. Davis[3], Alfred L. Garfall[2], J. Joseph Melenhorst[3,4], Russell Maxwell[1], W. Tristram Arscott[5], Amit Maity[1], Joshua A. Jones[1], John P. Plastaras[1], Edward A. Stadtmauer[2], Bruce L. Levine[3,4], Carl H. June[3,4], Michael C. Milone[3,4], and Ima Paydar[1]

- **Bridging RT is safe and feasible without worsening rates of severe CRS, neurotoxicity, or hematologic toxicity**
- **Bridging RT was not associated with change in OS or PFS**

- **RT administered <1 year (P < 0.002) and <100 days (P < 0.069) before apheresis was associated with lower in vitro proliferation during manufacturing; however, in vivo CART-BCMA expansion appeared similar**

Conclusions

- **Bridging RT appears to be SAFE and does not usually interfere with CART timeline**
- **PFS and OS are not negatively impacted, but selection confounds possible benefit**
- **RT squeezed between leukapheresis and lymphodepletion has been preferred timing, but intriguing role of consolidative and salvage RT in chemorefractory patients**
- **Patients who received comprehensive bridging and salvage RT appear to do better**
- **The A20 mouse model shows an ascopal effect that appears to synergize with CART19 using 4 Gy x 2**
  - Data not shown: there is strong tumor-associated antigen cross-presentation that appears to work through the cGAS/STING pathway