Identifying Biomarkers to Select Patients with Borderline Resectable and Locally Advanced Pancreatic Ductal Adenocarcinoma (BRPC, LAPC) for Radiotherapy (RT)

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Introduction

- BRPC and LAPC have poor prognosis in which surgery is the only curative treatment

- RT has a controversial role for BRPC and LAPC, with negative and positive data in recent years
- A high biologically effective dose of RT is required to achieve tumor ablation

- Since RT can impact the nearby gastrointestinal tract, the use of curative doses is constrained
- Previous studies have shown that RT following chemo is associated with better overall survival (OS)

Primary Aims

- There is an unmet need to identify biomarkers to select subpopulations of patients with BRPC and LAPC for RT

- Prior results indicated that CA19-9 response and lymphopenia grade associate with outcomes after RT
- Here, we investigated these markers and other clinical factors to identify biomarkers that may aid the decision to use RT for BRPC and LAPC
- We hypothesized that lymphopenia grade and CA19-9 normalization would show to be independent predictors of OS

Methods

- Conducted a retrospective study to analyze patients who received chemotherapy followed by RT for BRPC or LAPC between 2015 and 2020
- Patients evaluated as a subset from a larger cohort of 454 patients
- RT dates and lowest absolute lymphocyte counts (ALC) during RT periods were extracted from medical records
- CA19-9 normalization = minimum CA19-9 value between the start of chemo and 6 months post-chemo < 40 U/mL
- Lymphopenia grade >2 = patient ALC fell below 0.5 K/uL during radiation
- Associations between variables were tested using Log-rank and Wilcoxon survival analyses
- Variables with a p value of <.2 in univariate analysis were used in a multivariate Cox Proportional Hazard survival analysis test to further determine significance

Results
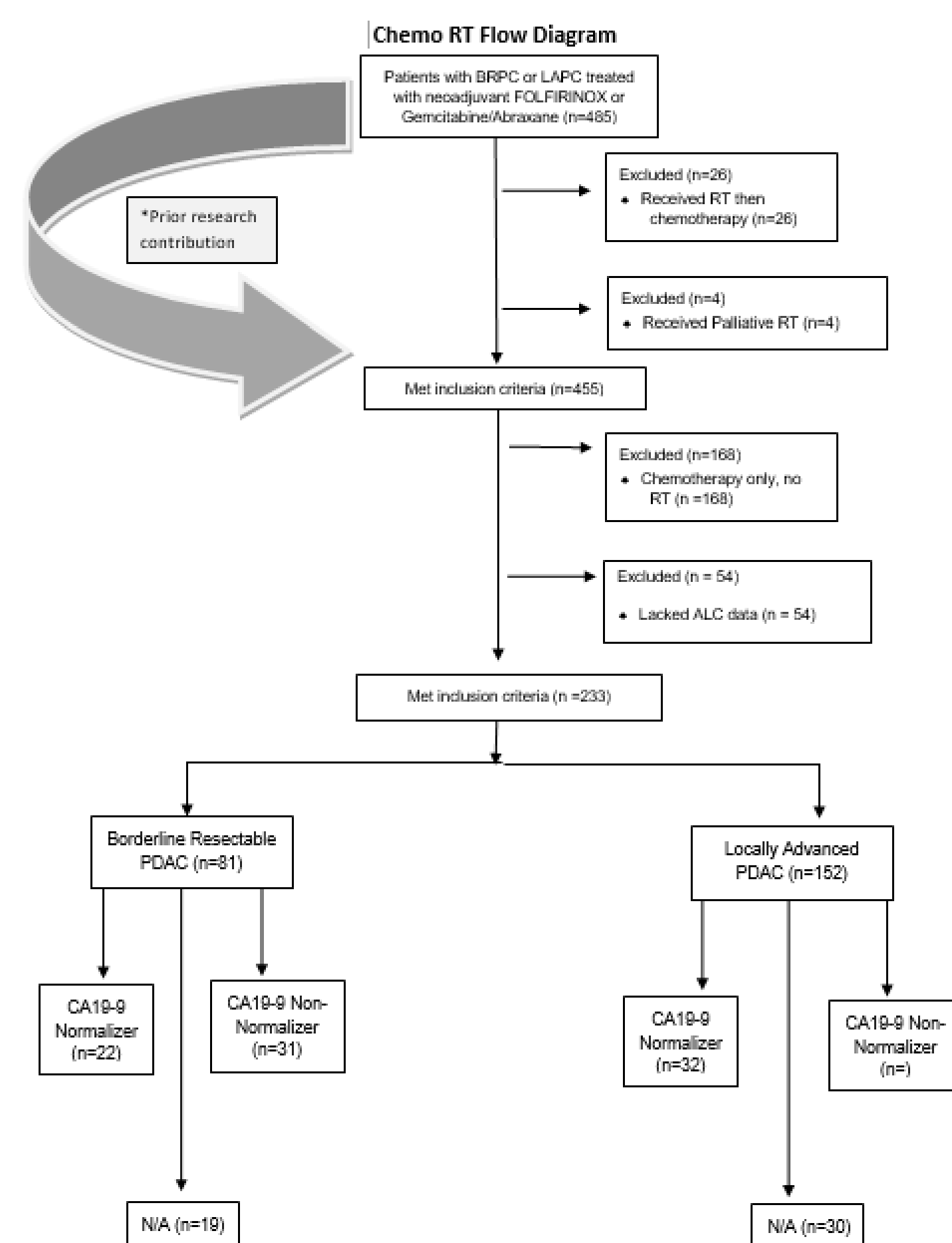
Fig 1. Workflow showing how the data set of N = 233 was created along with the number of patients within each subset of tumor type and CA19-9 normalization.

| Variable	Median OS (months)	p-value
CA19-9 Normalization	Normalizer = 19.3 Non-normalizer = 11.5	0.015
Non-normalizers Receive Surgery?	Surgery = 25.4 No surgery = 8.84	0.0001
Radiation Type	Stereotactic Body RT: 22.7 Volumetric Modulated Arc Therapy: 19.1 3-D Plan: 11.5 Intensity-Modulated RT: 10.1	0.019
Tumor Type (Lymphopenia grade>2)	BRPC: 23.4 LAPC: 11.6	0.003

Table 1. The above four variables showed to be significantly associated with overall survival in the patient population (p<.05). Log-rank and Wilcoxon tests were used to evaluate significance.
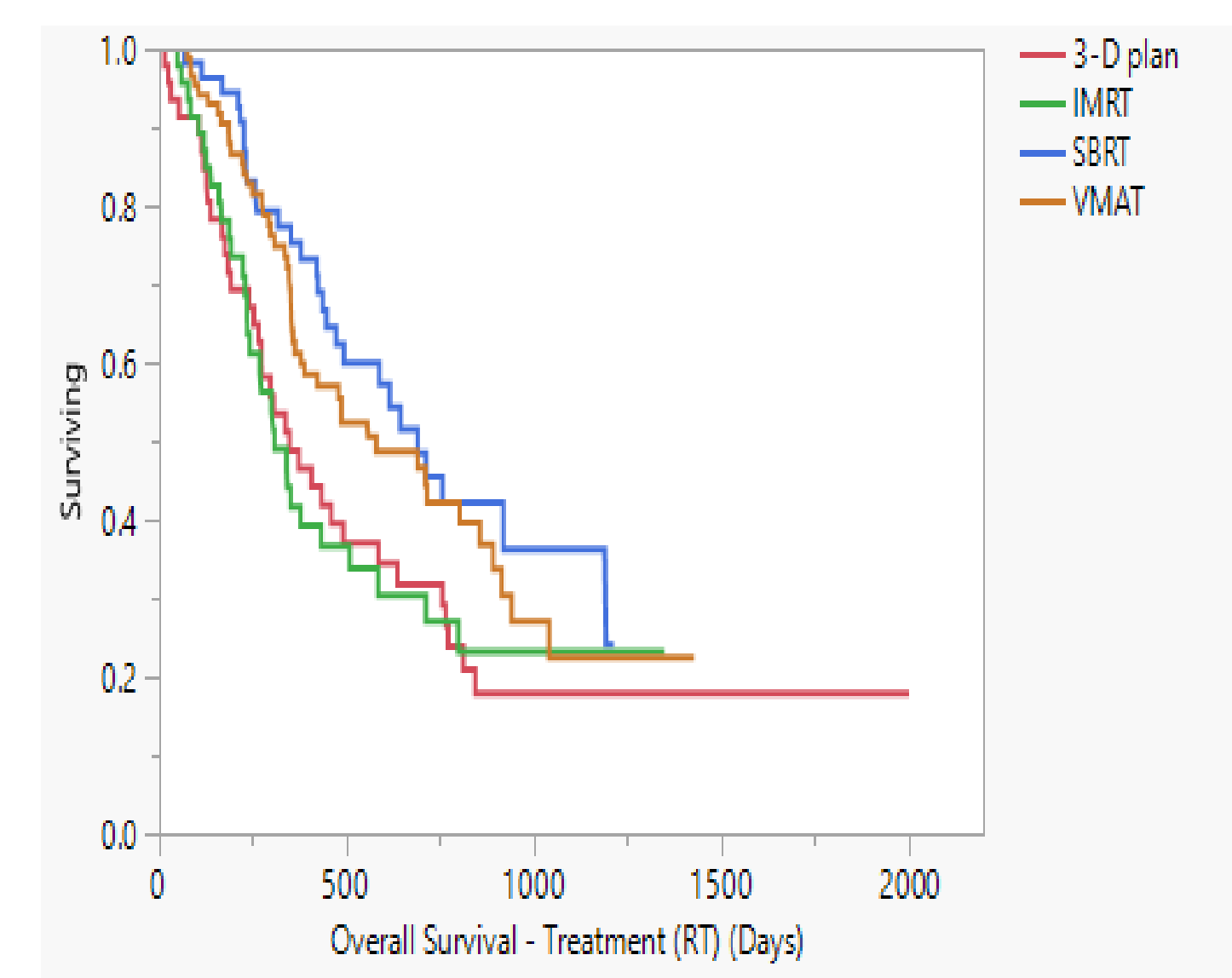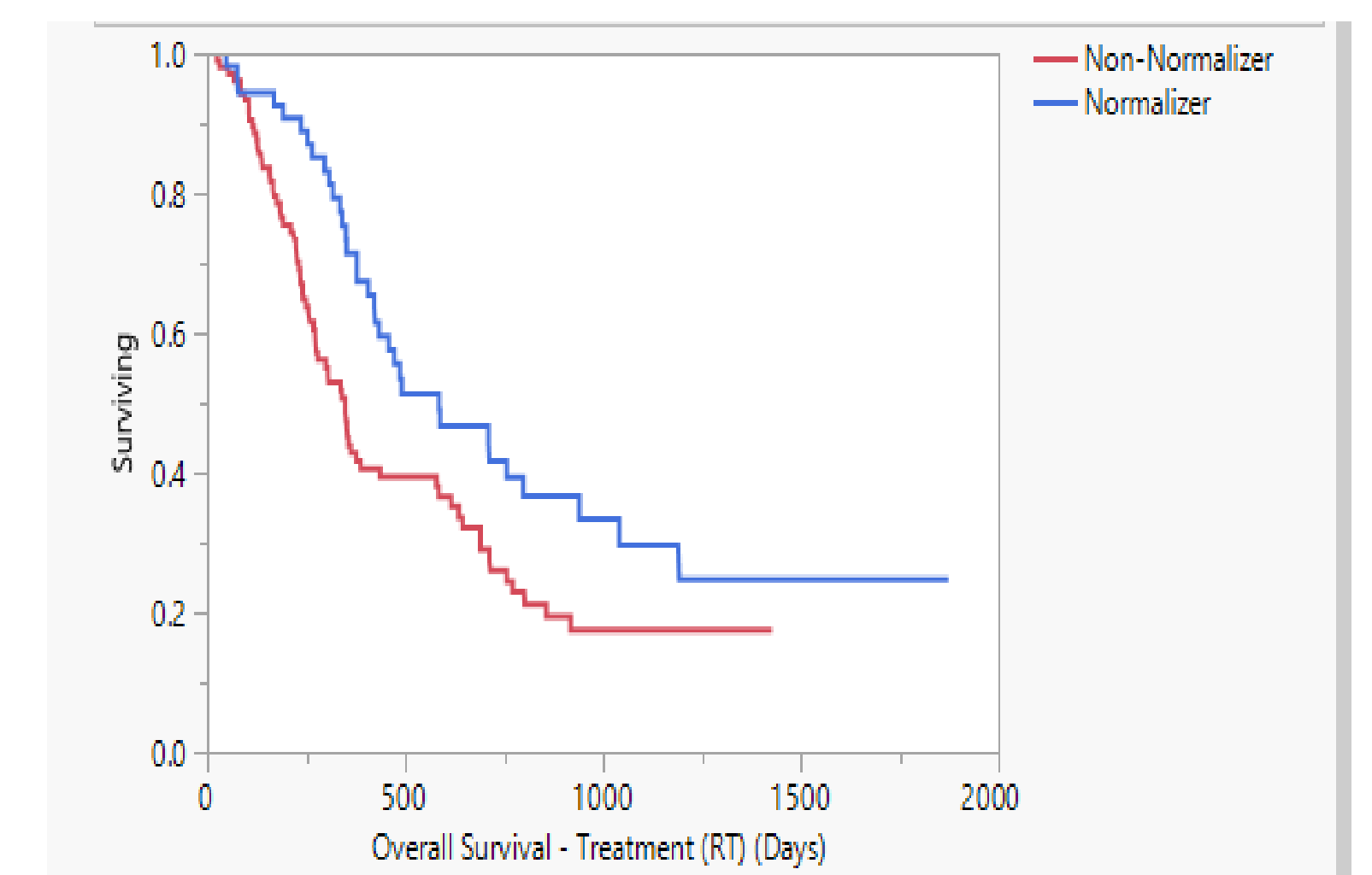

Fig 2. Survival plot for different radiation types.
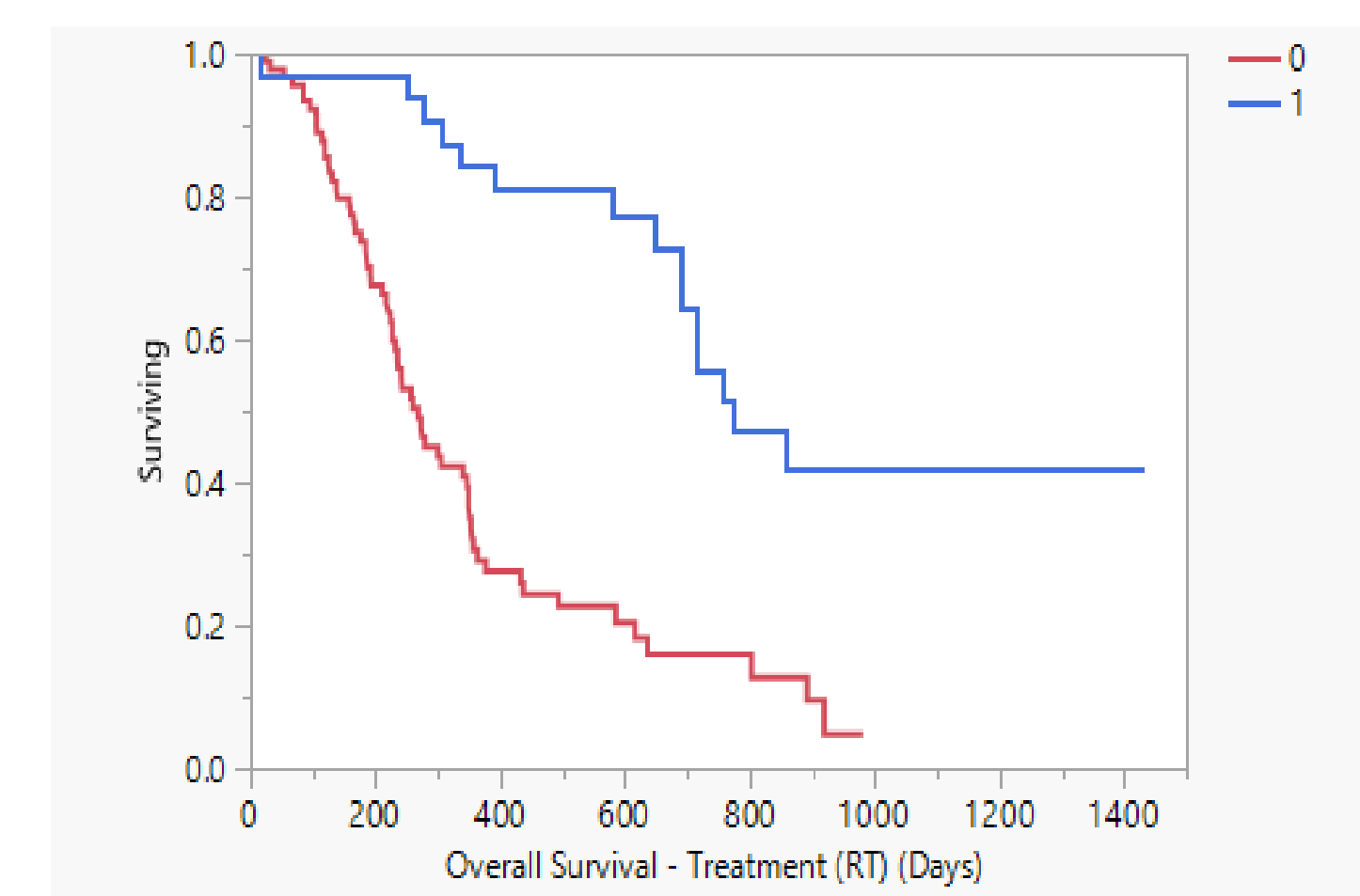
Fig 3. Survival plot for non-normalizers surgery vs non-surgery (0 = no surgery, 1 = surgery).
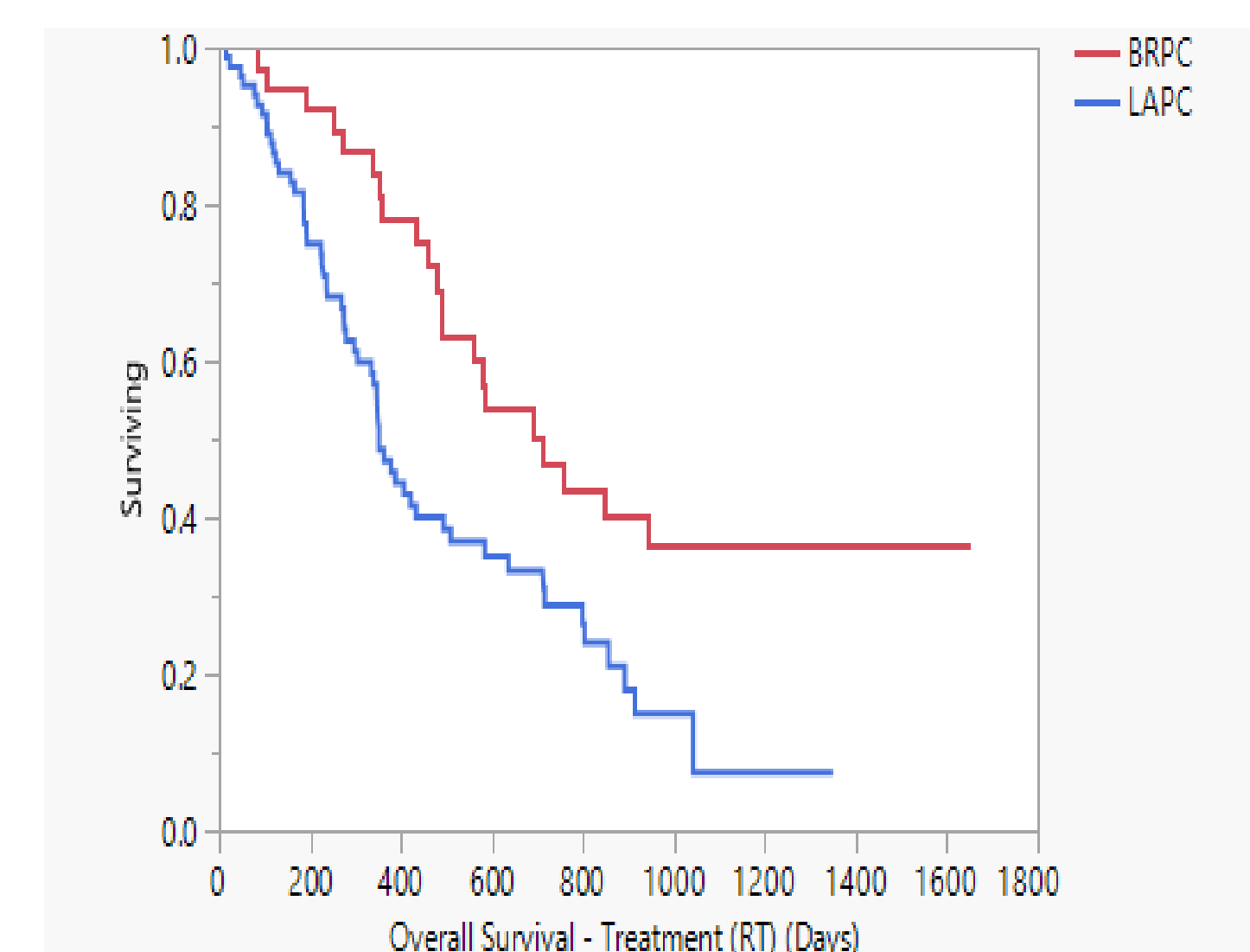
Fig 4. Survival plot for different tumor types of patients with lymphopenia grade >2.

Fig 5. Survival plot for CA19-9 normalizers compared to non-normalizers.

Variable	Hazard Ratio (95% Confidence Interval)	P-value
CA19-9 Normalization	Norm: 0.489 (0.318-0.745) Non: 2.04 (1.33-3.14)	0.00012
Surgery or No Surgery?	Surgery: 0.190 (0.106-0.342) No surgery: 5.25 (2.93-9.42)	0.0001
Radiation Type	IMRT: 0.496 (0.279-0.883) SBRT: 0.359 (0.183-0.703) VMAT: 0.402 (0.237-0.680) 3-D Plan: 2.49 (1.47-4.21)	0.0032

Table 2. The above three variables showed to be significant (p<.05) in the multivariate Cox Proportional Hazard Model.

Conclusions

- Preliminary analysis indicated CA19-9 to be a significant variable associated with OS as predicted
- Lymphopenia grade did not show to be significant as an independent variable
- However, there was a significant difference in BPRC vs LAPC OS for patients with lymphopenia grades >2
- Additional prospective trials are needed to evaluate the ability of these factors to personalize treatment and solidify stable biomarkers

References

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