

UPDATE ON THE **STREXIT** STUDY OF PRIMARY RPS

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Semi-Annual Meeting of TARPSWG
San Diego, CA March 27, 2019



UNIVERSITY OF
TORONTO

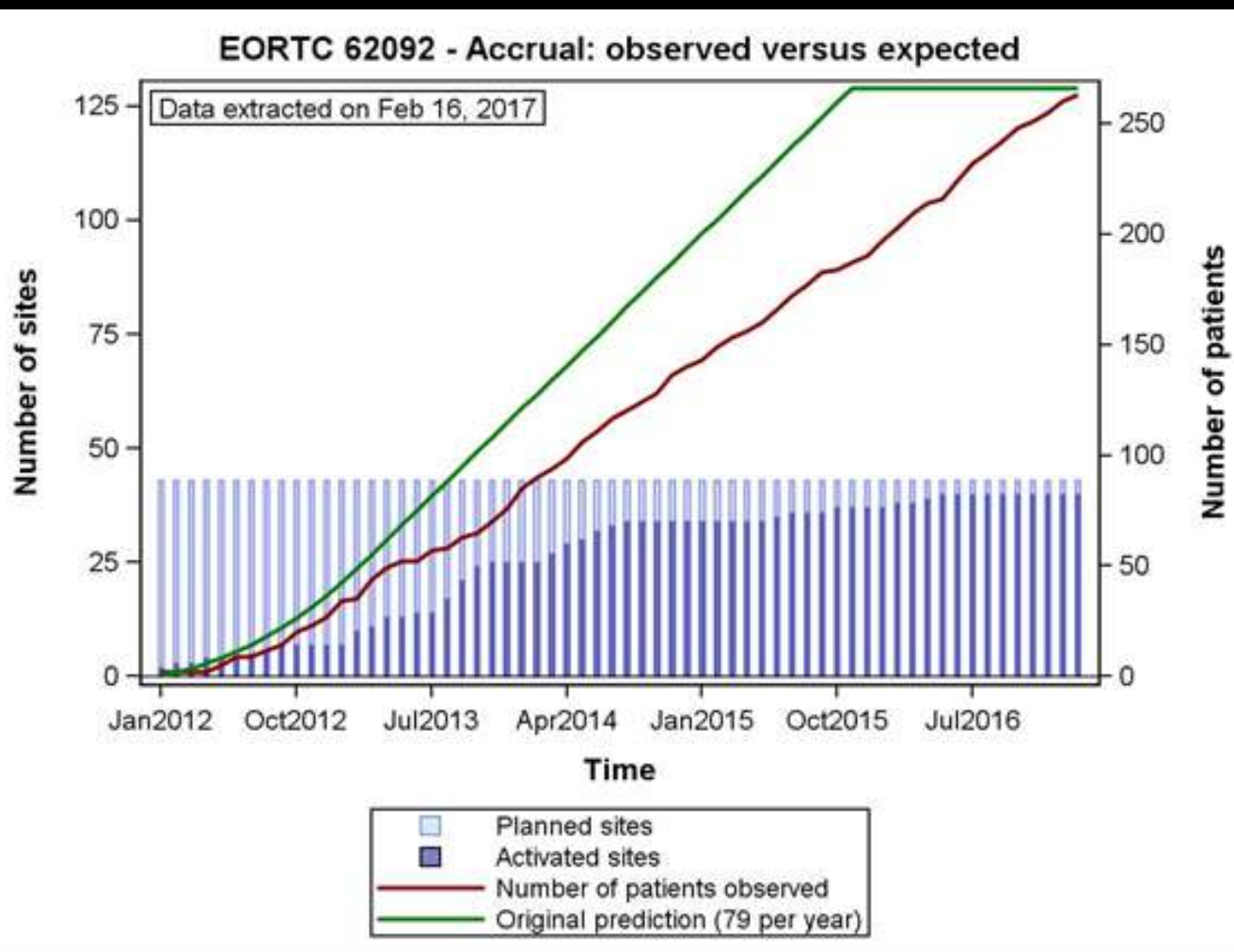


**TORONTO
SARCOMA**

ACCRUAL: 266 PATIENTS OVER 25 SITES

(JAN 2012 – APRIL 2017)

Institution Name	All patients (N=266) N (%)
IRCCS - Ist Tumori	50 (18.8)
Gustave Roussy	44 (16.5)
Mount Sinai Hosp. *	25 (9.4)
Royal Marsden Hosp.	17 (6.4)
Centre Leon Berard	14 (5.3)
NKI / AVL	13 (4.9)
Oslo Univ Hosp *	13 (4.9)
Institut Bergonie	12 (4.5)
M.S-K.C.Ctr.Warsaw	11 (4.1)
Inst. Oncol. Veneto	8 (3.0)
Institut Curie	8 (3.0)
Dana Farber Canc Ins *	7 (2.6)
C.Rifer Onc Aviano	5 (1.9)
U.Z. Gasthuisberg	5 (1.9)
Herlev Copenhag.	4 (1.5)
UHB Queen Elisabeth	4 (1.5)
CHUM - Notre-Dame *	3 (1.1)
UMC Groningen	3 (1.1)
Univ Med Ctr Leiden	3 (1.1)
Humanitas Rozzano	2 (0.8)
Karolinska - Solna *	2 (0.8)
RU Nijmegen	2 (0.8)
UH Bristol NHS	2 (0.8)
Weston Park Hospital	2 (0.8)
Christie Manchester	1 (0.4)



THE STREXIT STUDY

Rationale:

Enrollment onto STRASS was

- challenging, despite commitment of individual investigators/centers
- potentially biased

Questions:

Will results of STRASS be generalizable?

How can we improve recruitment onto the next trial?

THE STREXIT STUDY

AIMS

- describe a contemporaneous group of patients managed at the same centers, but **not** enrolled on STRASS
- compare baseline features and outcomes to those of STRASS patients
- prepare to set the results of STRASS in context
- gain insight into the challenges of recruiting patients onto neoadjuvant RPS studies

METHODS

Inclusion Criteria (Center):

- at least one patient on STRASS
- prospective DB
- responded to invitation to participate

Exclusion Criteria (Center):

- unable to identify RPS patients from a prospectively maintained DB

METHODS

Inclusion Criteria (Patients):

- primary RPS
- no distant metastases at presentation
- underwent resection at Sarcoma reference center
- consecutive cases Jan 2012- April 2017

Exclusion Criteria (Patients):

- histologies excluded from STRASS

PARTICIPATING CENTERS

10 centres

≥1 patient on STRASS1

prospective RPS data base

- Royal Marsden, London
- Istituti Nazionale dei Tumori, Milano
- Gustave Roussy, Paris
- Marie Curie, Paris
- MSKC-Ctr, Warsaw
- Mount Sinai/Princess Margaret, Toronto
- NKI, Amsterdam
- Dana Farber, Boston
- Istituto Bergonié
- LUMC, Leiden

STREXIT – PART1

Why Primary Retroperitoneal Sarcoma Patients Undergoing Treatment at STRASS Institutions Did Not Enroll in STRASS: The STREXIT Study from EORTC STBSG and TARPSWG

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THE STREXIT STUDY

AIMS

- describe a contemporaneous group of patients managed at the same centers, but **not** enrolled on STRASS
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BASELINE CHARACTERISTICS

PATIENT CHARACTERISTICS: STREXIT vs. STRASS

	STREXIT	STRASS
n	836	266
Age (years) Median, IQ range	62 (52-70)	61 (52-68)
F/M (%F)	397/439 (47.5%)	128/138 (48.1%)
Follow-up (months) Median, 95% CI	36 (34-39)	43 (29-59)
WHO Performance Status		
0		210 (78.9%)
1		55 (20.7%)
2		1 (0.4%)

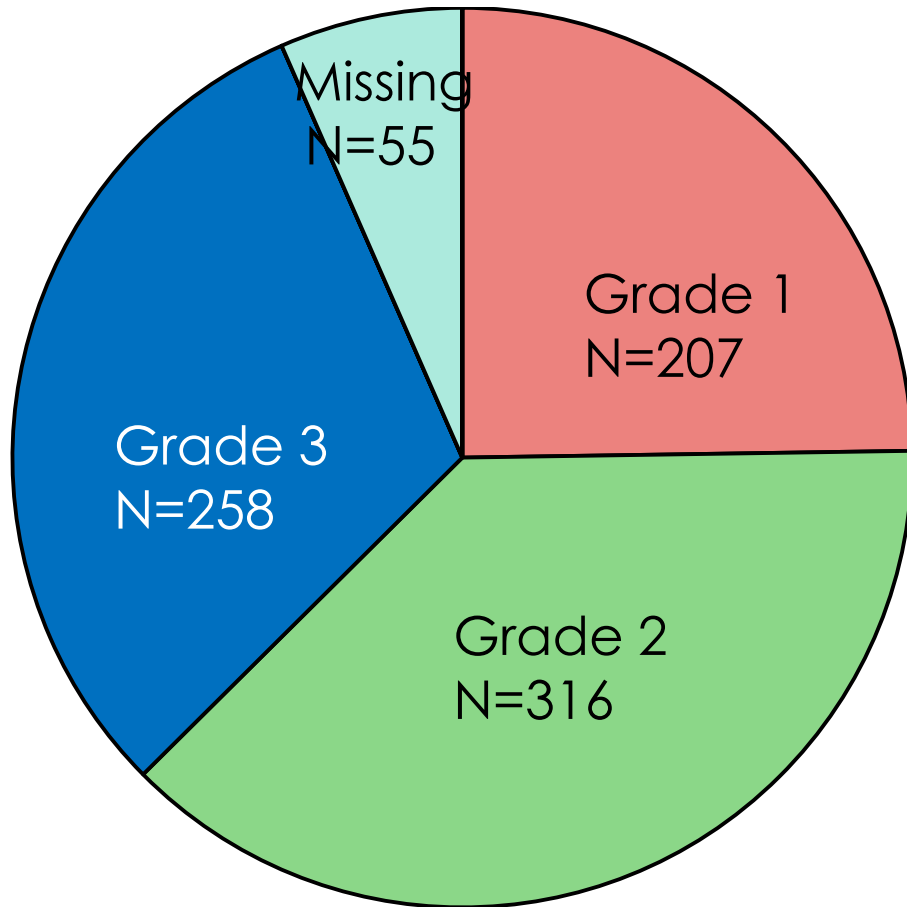
BASELINE CHARACTERISTICS

TUMOR CHARACTERISTICS : STREXIT vs. STRASS

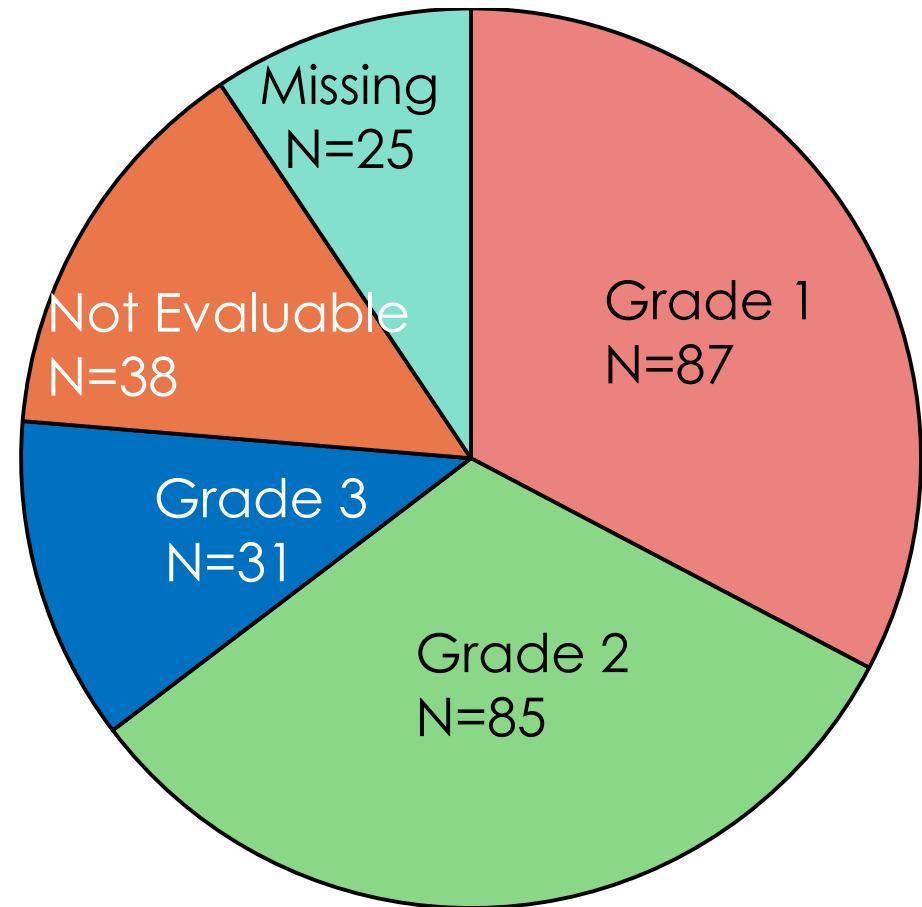
	STREXIT	STRASS
n	836	266
Size (cm) Median, IQ range	21 (14 - 30)	16 (12 - 21)*
Grade		
1 (n, %)	207 (26.5%)	87 (32.7%)
2 (n, %)	316 (40.5%)	85 (32.0%)
3 (n, %)	258 (33.0%)	31 (11.7%)*
Not evaluable		38 (14.3%)
Missing	55 (6.6%)	25 (9.4%)
Multifocality (n, %)	42 (5.0%)	14/251 (5.6%)
Rupture	30 (3.6%)	6/251 (2.4%)

DISTRIBUTION BY GRADE

STREXIT, n=834



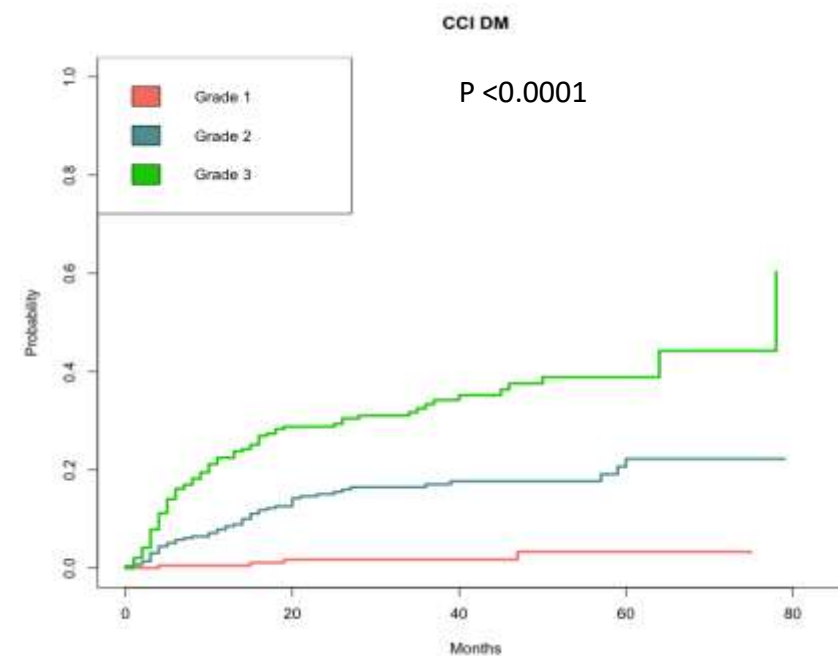
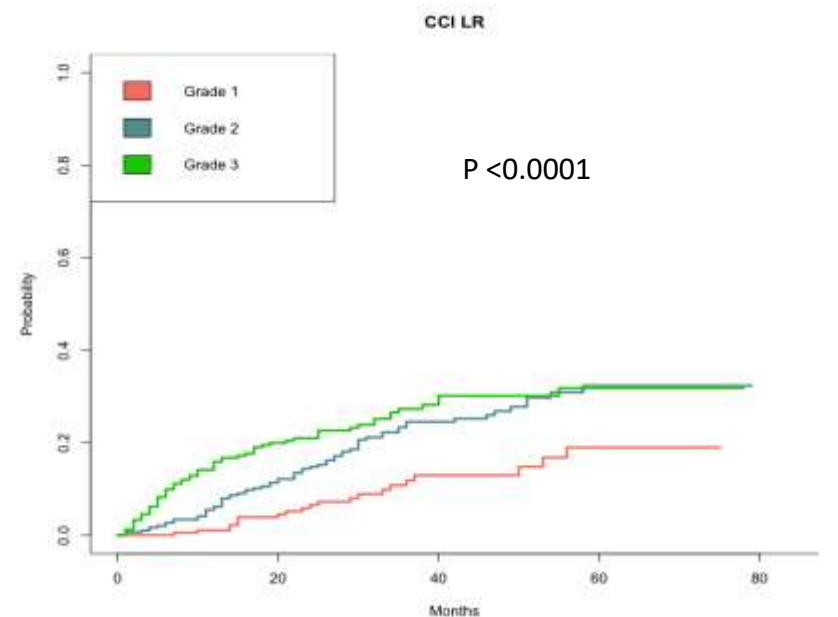
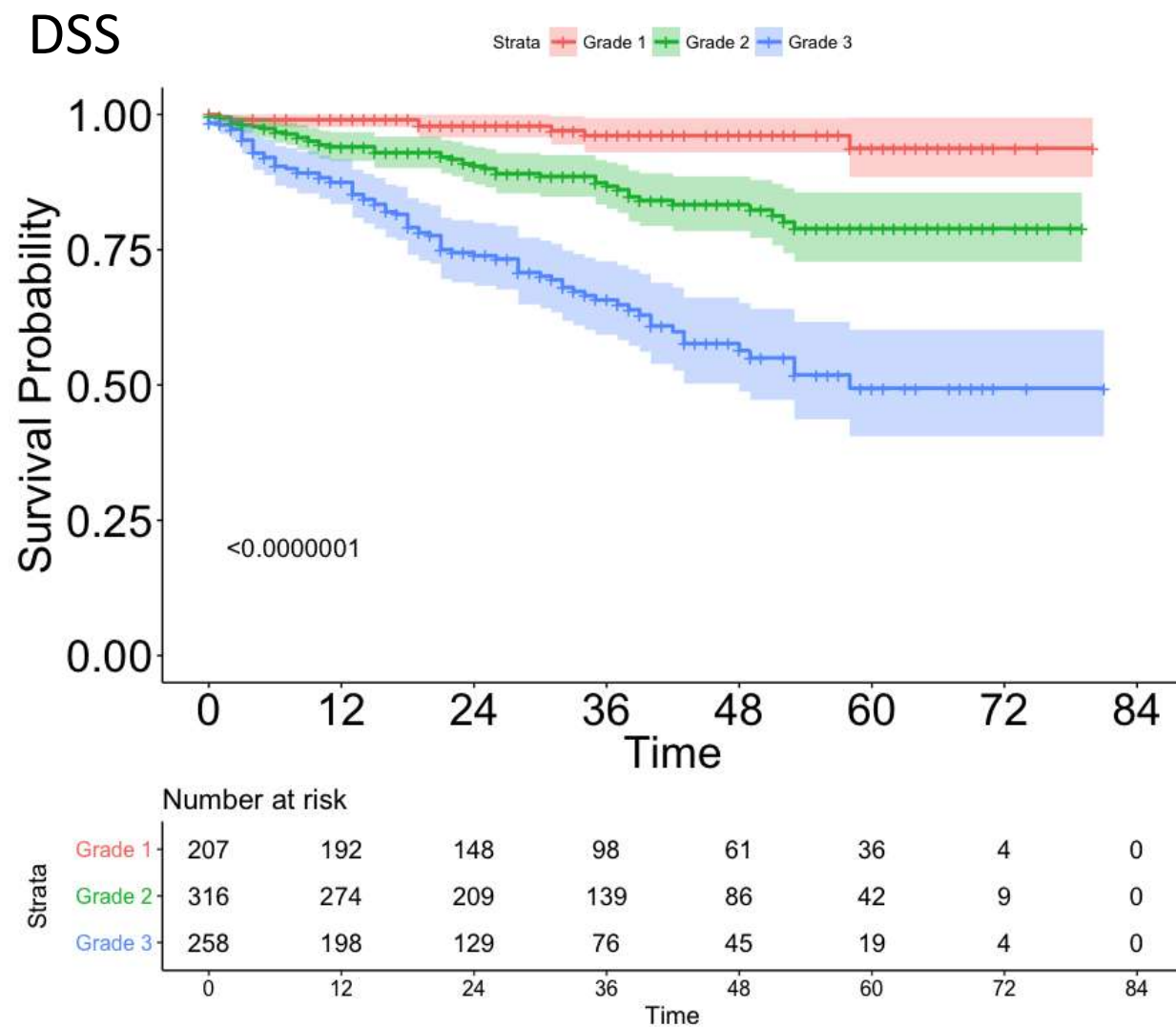
STRASS, n=266



- 10 centres that enrolled ≥ 1 patient on STRASS, prospective DB
- primary RPS, no distant mets, resected 2012-2017

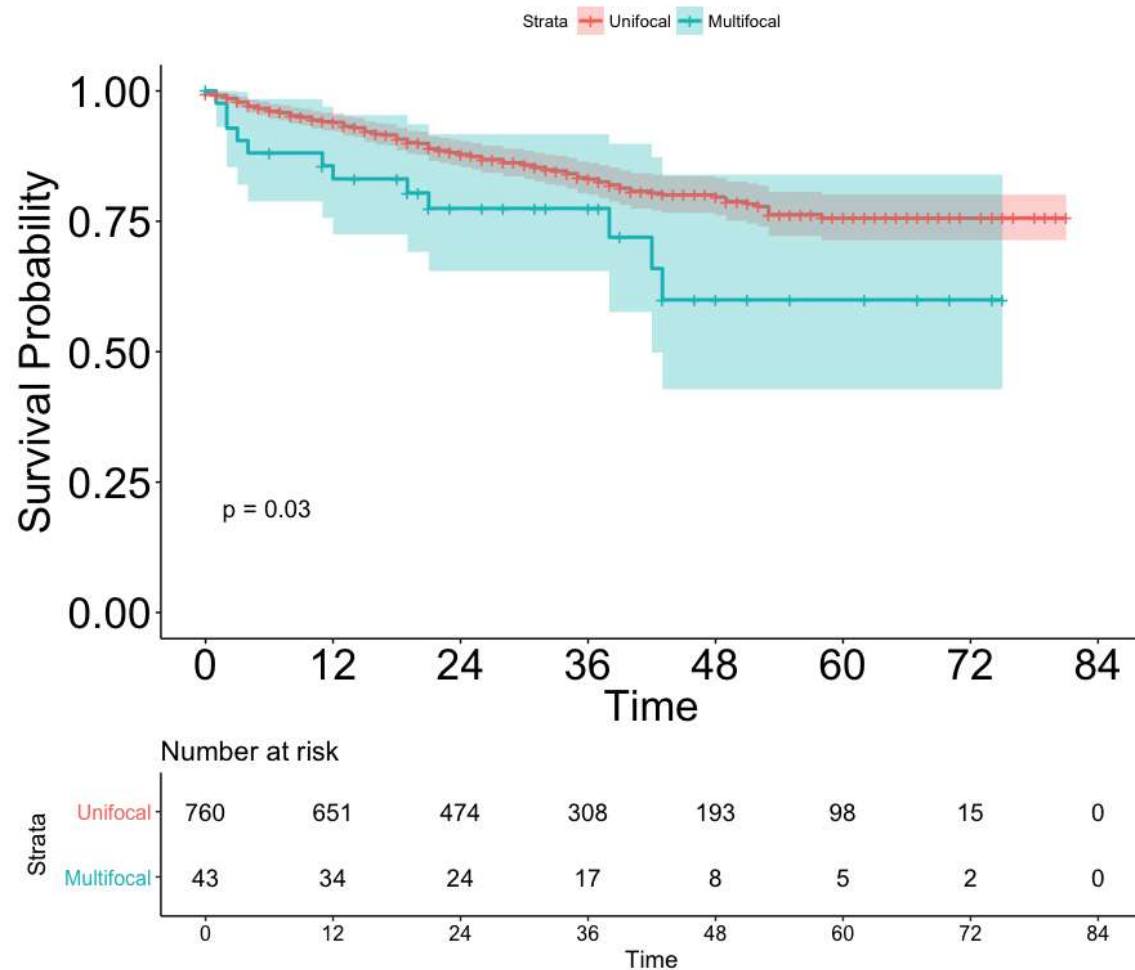
STREXIT

Outcomes by Grade

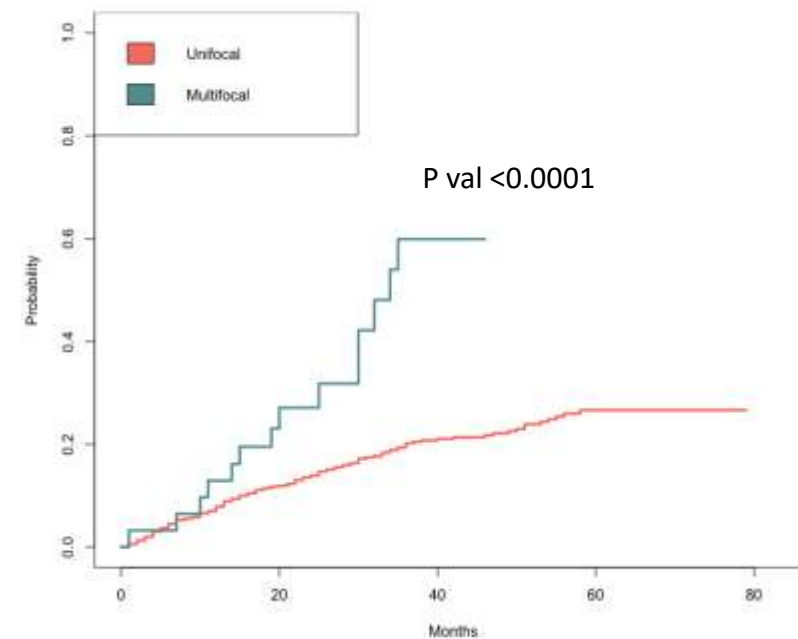


Outcomes by Focality

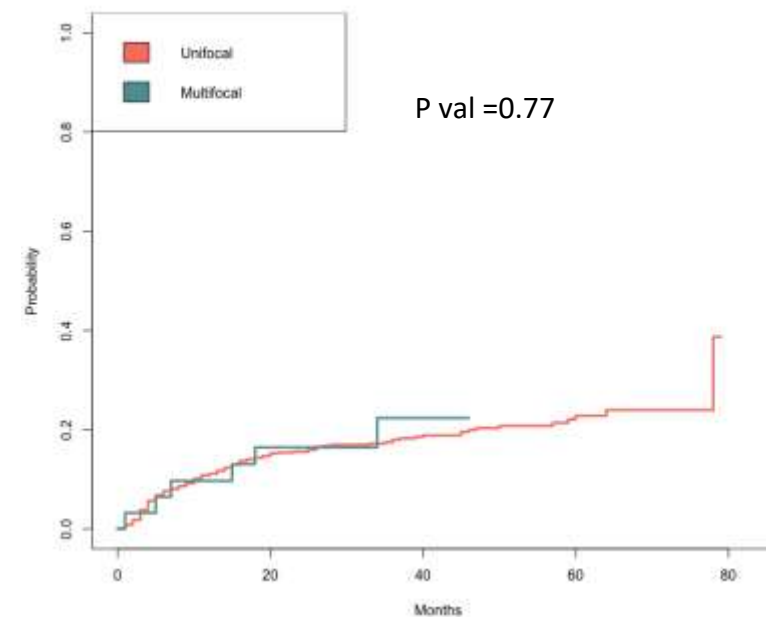
DSS



CCI LR



CCI DM



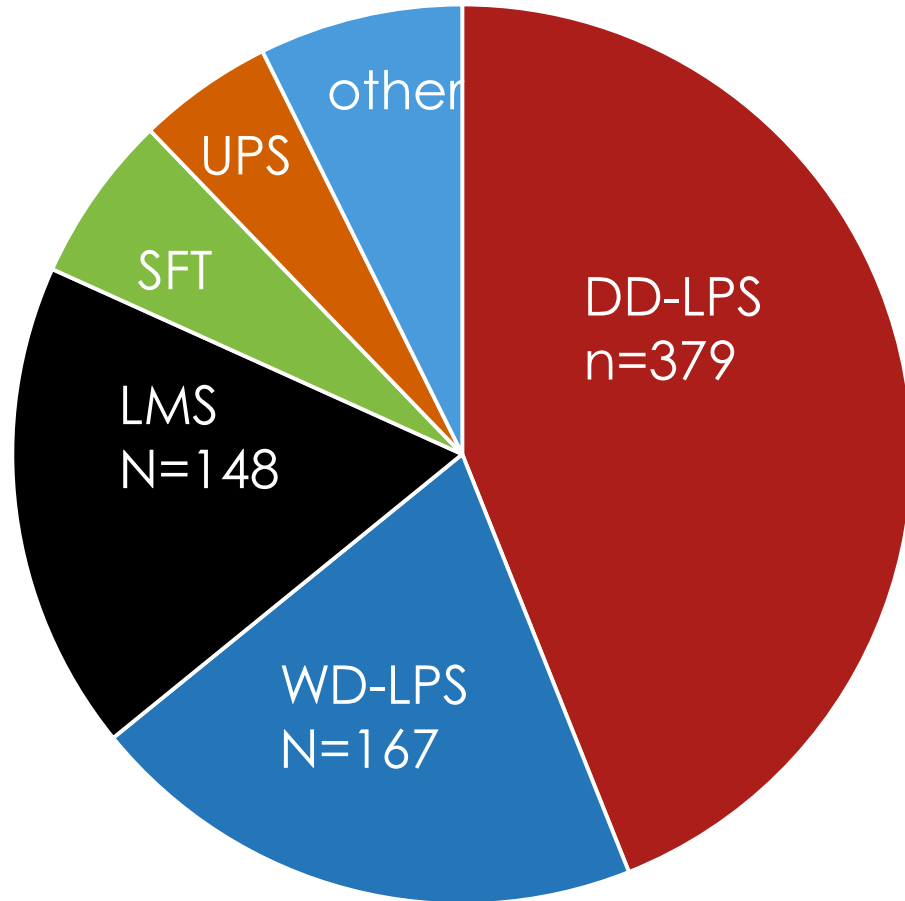
BASELINE CHARACTERISTICS

TUMOR CHARACTERISTICS: STREXIT vs. STRASS

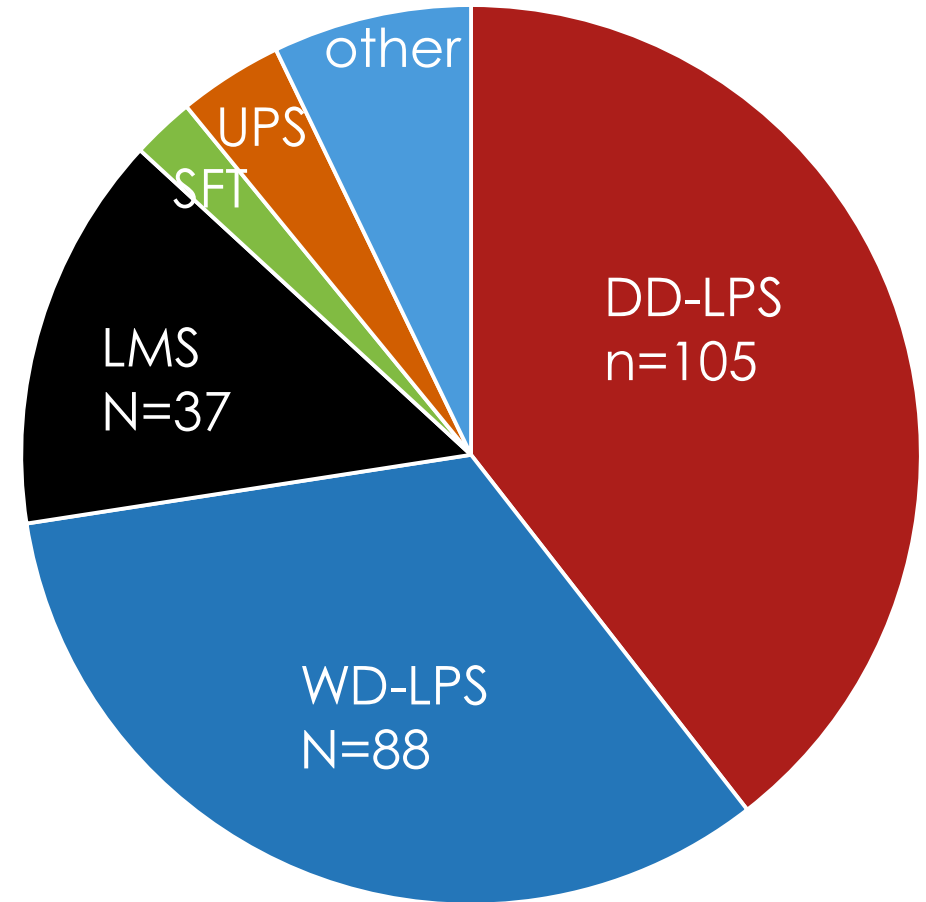
	STREXIT	STRASS
n	836	266
Histologic Subtype		
WD-LPS (n, %)	167 (20%)	88 (33.1%)*
DD-LPS (n, %)	379 (45.3%)	105 (39.5%)
LMS (n, %)	148 (17.7%)	38 (14.3%)
SFT (n, %)	47 (5.6%)	6 (2.3%)
UPS (n, %)	38 (4.5%)	10 (3.8%)
MPNST (n, %)	22 (2.6%)	3 (1.1%)
Other (n, %)	35 (4.2%)	16 (6.0%)

HISTOLOGIC SUBTYPE

STREXIT, n=834



STRASS, n=266



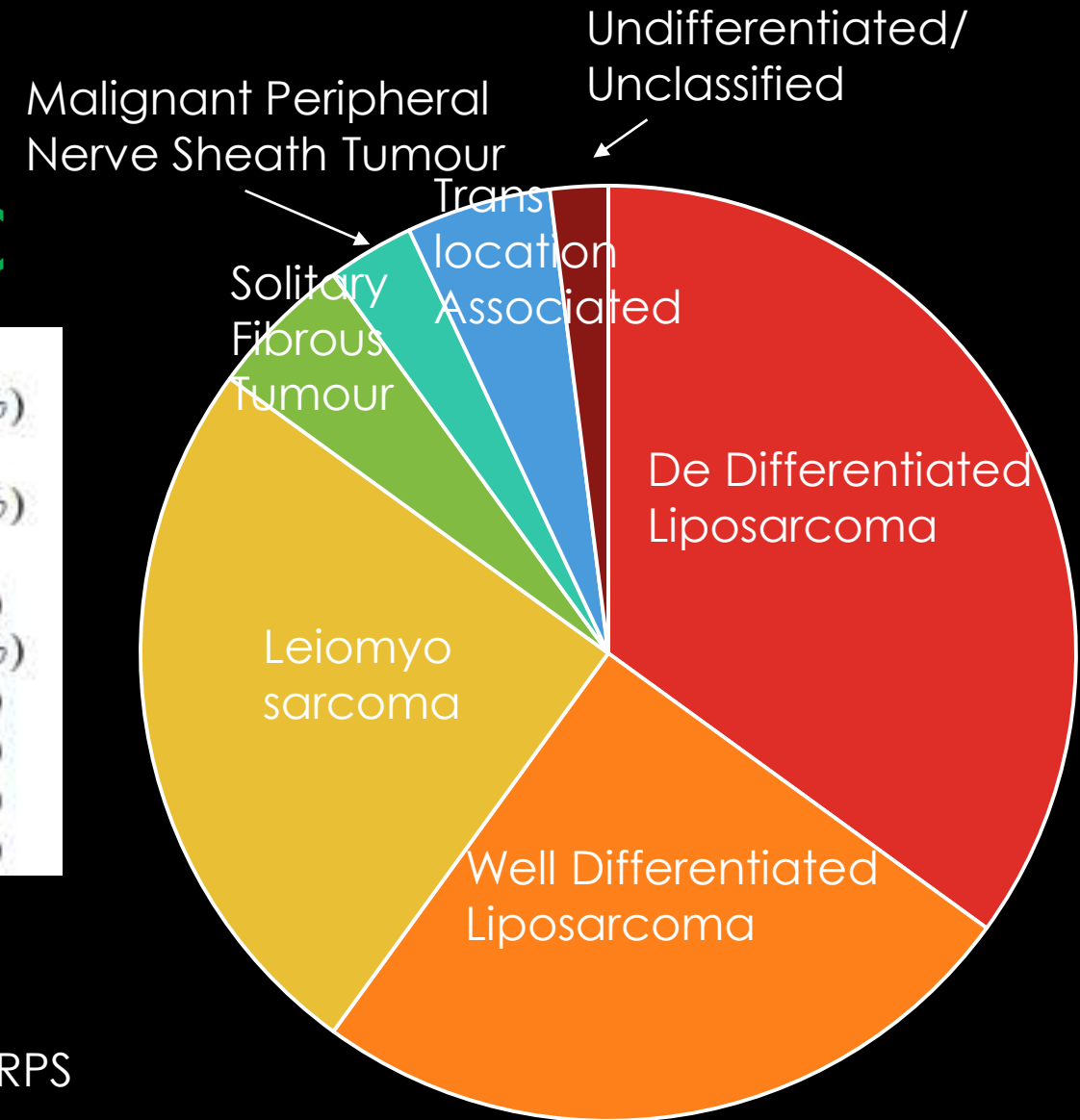
- 10 centres that enrolled ≥ 1 patient on STRASS, prospective DB
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Histology-Specific outcomes

Histologic Subtypes @ MSKCC

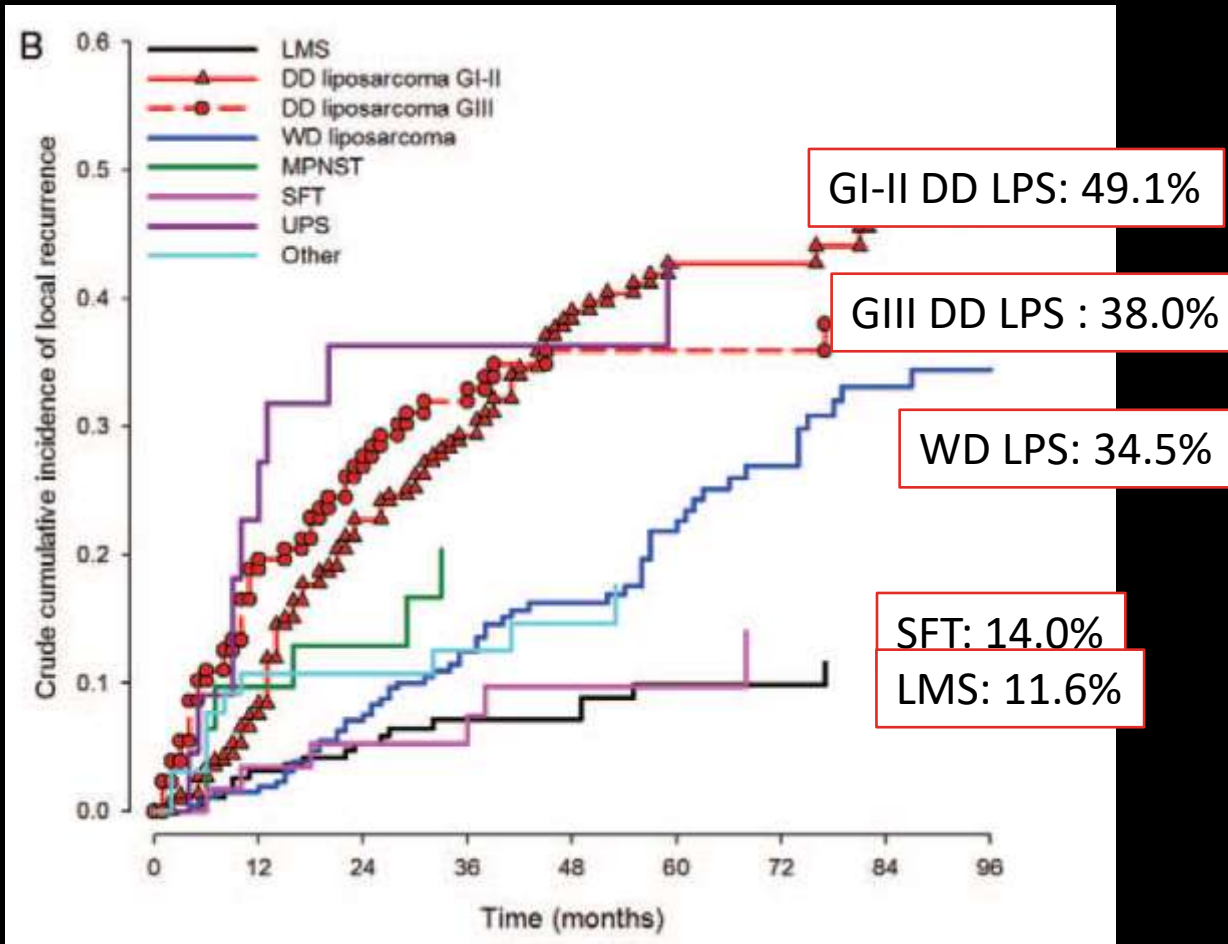
Histology*	
Liposarcoma: well-differentiated and myxoid	186 (28%)
Liposarcoma: dedifferentiated, round cell and pleomorphic	213 (32%)
Low-grade leiomyosarcoma	18 (3%)
High-grade leiomyosarcoma	132 (20%)
SFT	33 (5%)
Malignant peripheral nerve sheath tumor	23 (3%)
Translocation-associated and other	34 (5%)
Not otherwise specified	35 (5%)

Marcus C. B. Tan, MBBS,* Murray F. Brennan, MD,* Deborah Kuk, ScM,† Narasimhan P. Agaram, MBBS,‡
Cristina R. Antonescu, MD,‡ Li-Xuan Qin, PhD,† Nicole Moraco, MA,* Aimee M. Crago, MD, PhD,*
and Samuel Singer, MD*

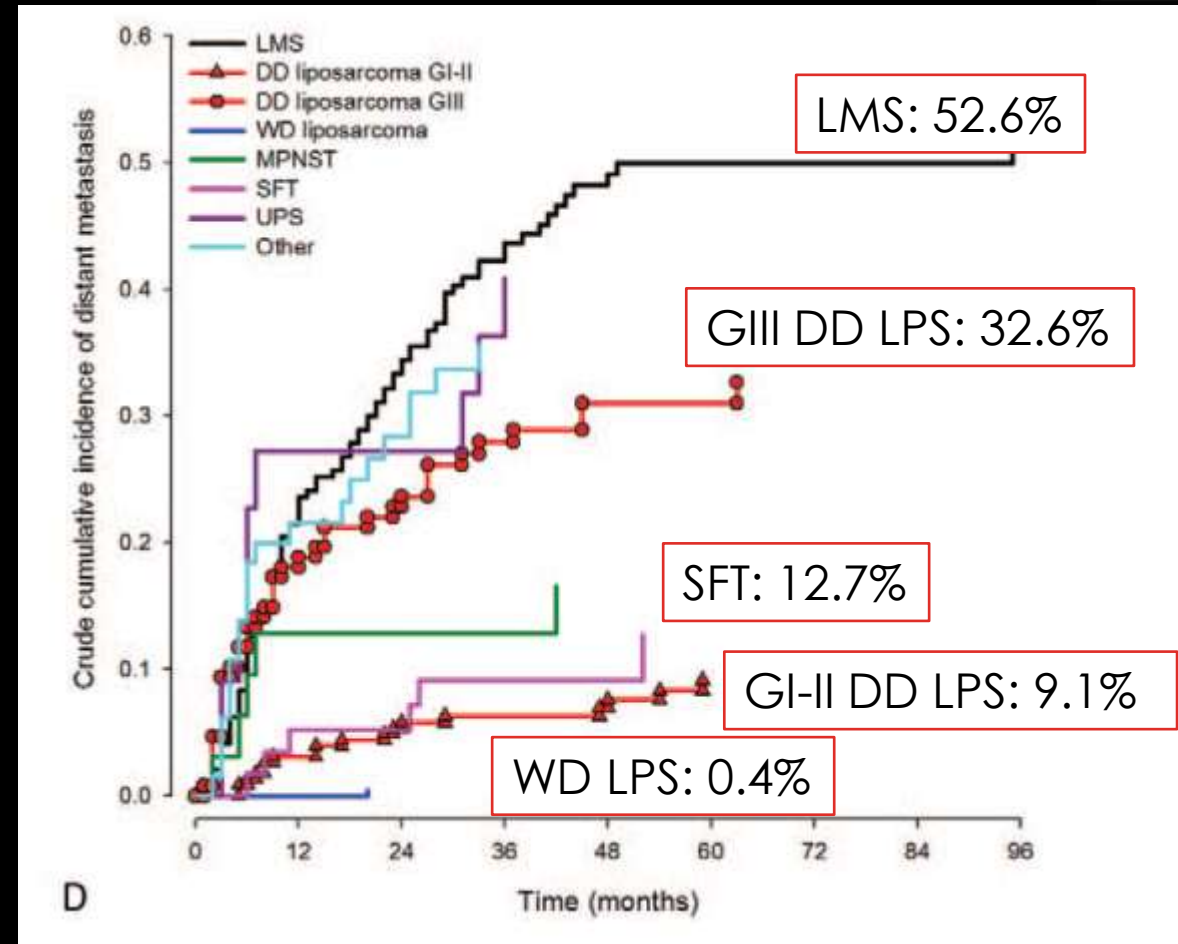


STRASS - Potential Limitations

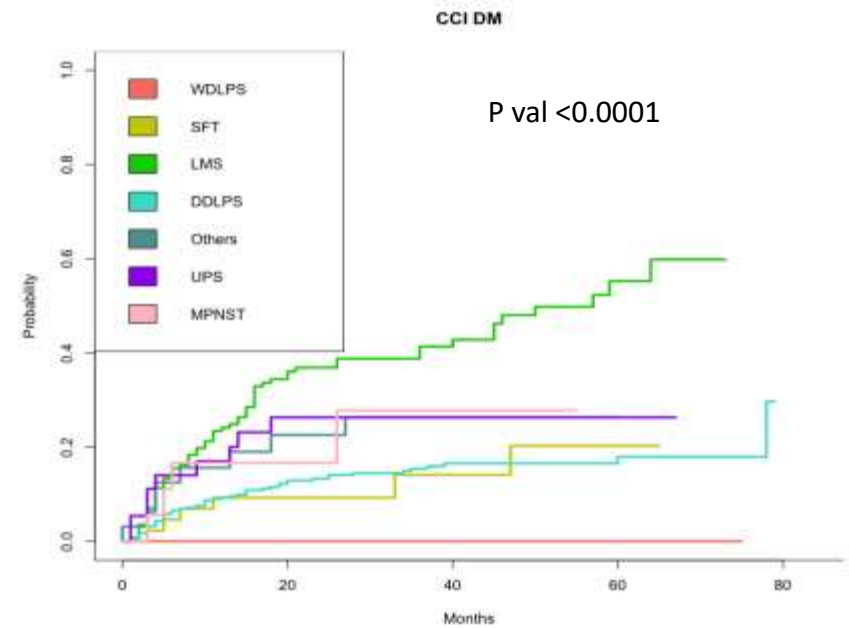
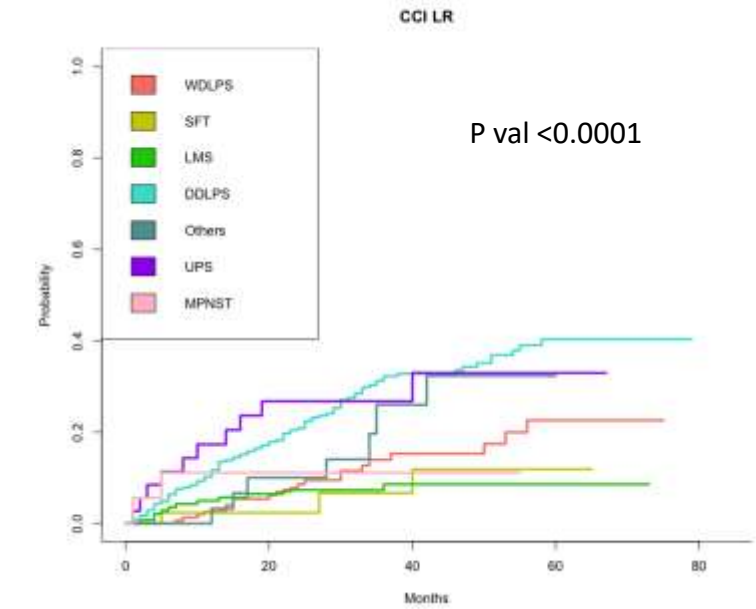
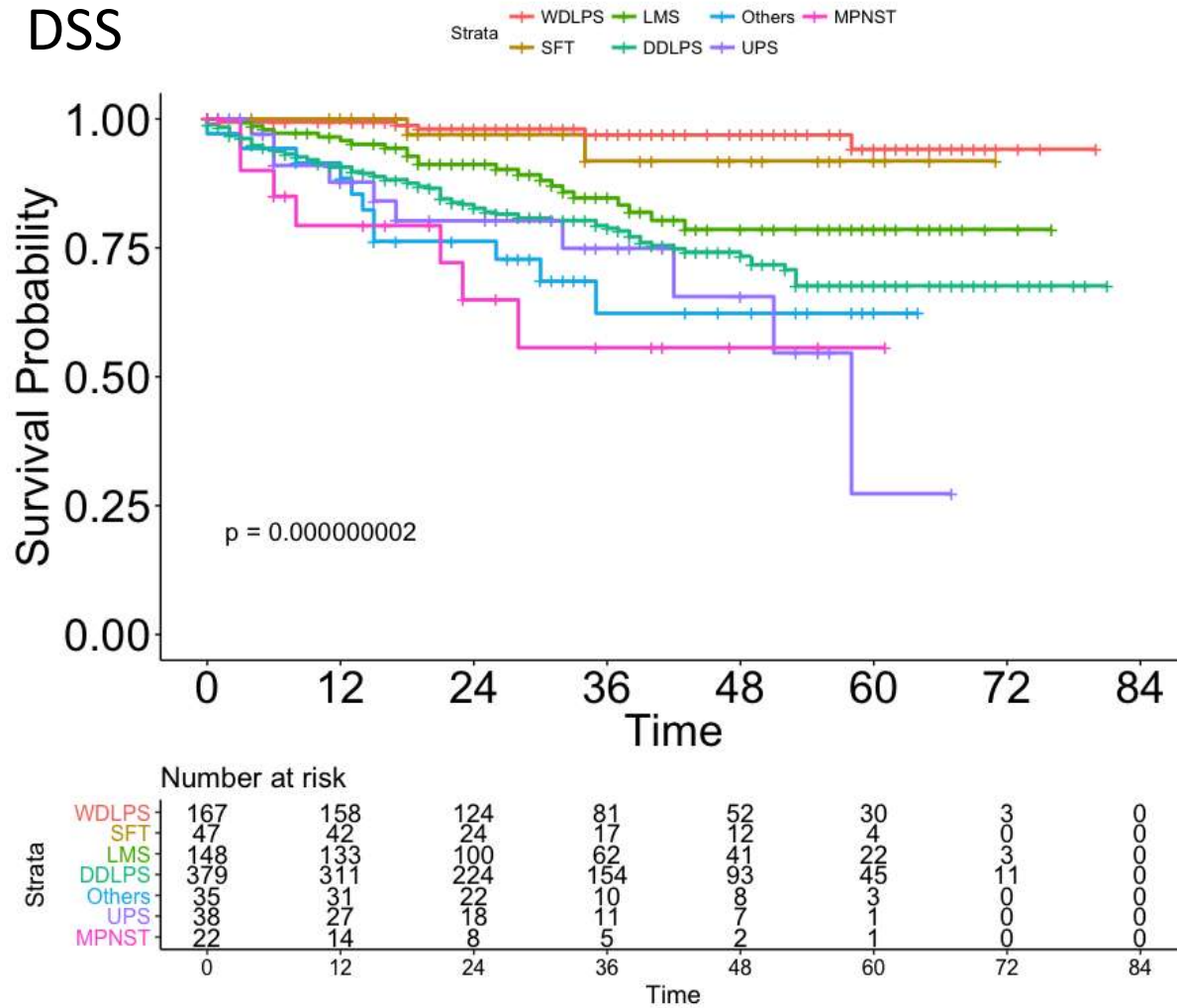
LOCAL RECURRENCE BY HISTOLOGY (1007 PTS)



DISTANT RECURRENCE BY HISTOLOGY (1007 PTS)



Outcomes by Histology



BASELINE CHARACTERISTICS

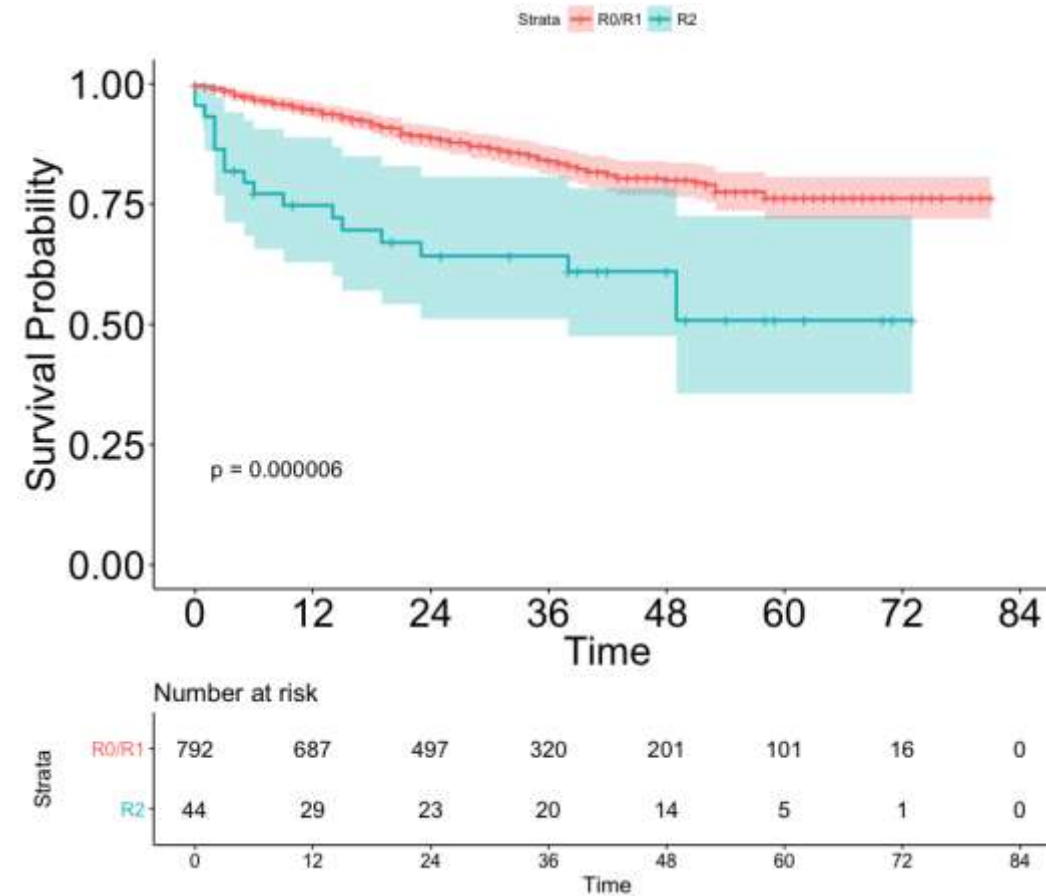
TREATMENT: STREXIT vs. STRASS

	STREXIT	STRASS
n	836	266
Preop XRT (n, %)	141 (16.9%)	127 (47.7%)
Postop XRT (n, %)	2 (0.2%)	
Preop CT (n, %)	96 (11.5%)	
CT, any (n, %)	118 (14.1%)	
Resection (n, %)	836 (100%)	251 (94.3%)
R2 Resection (n, % of resected)	42 (5.0%)	2 (0.08%)*

STREXIT

Survival by R Status

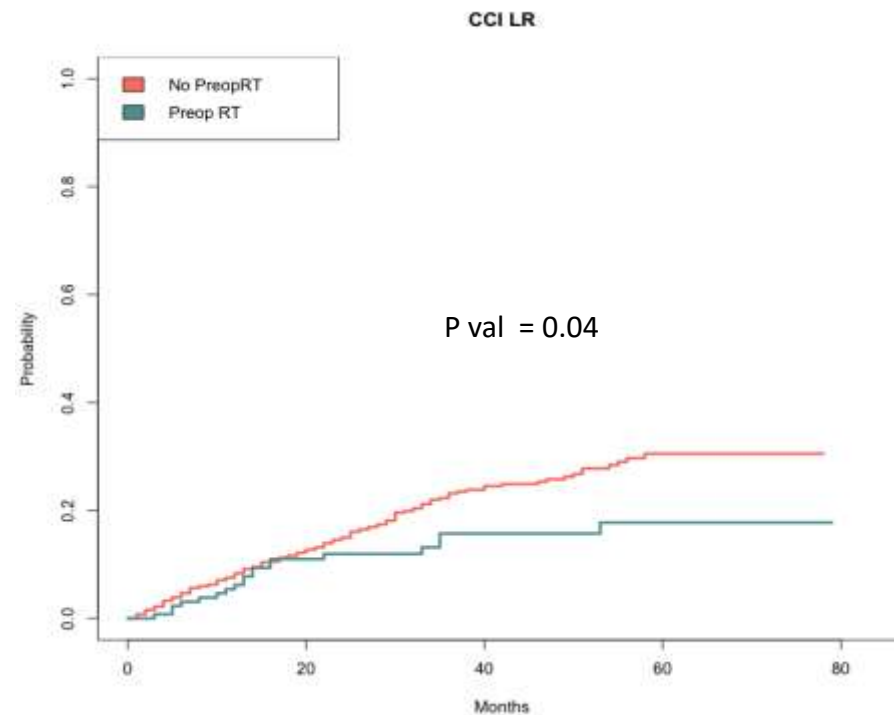
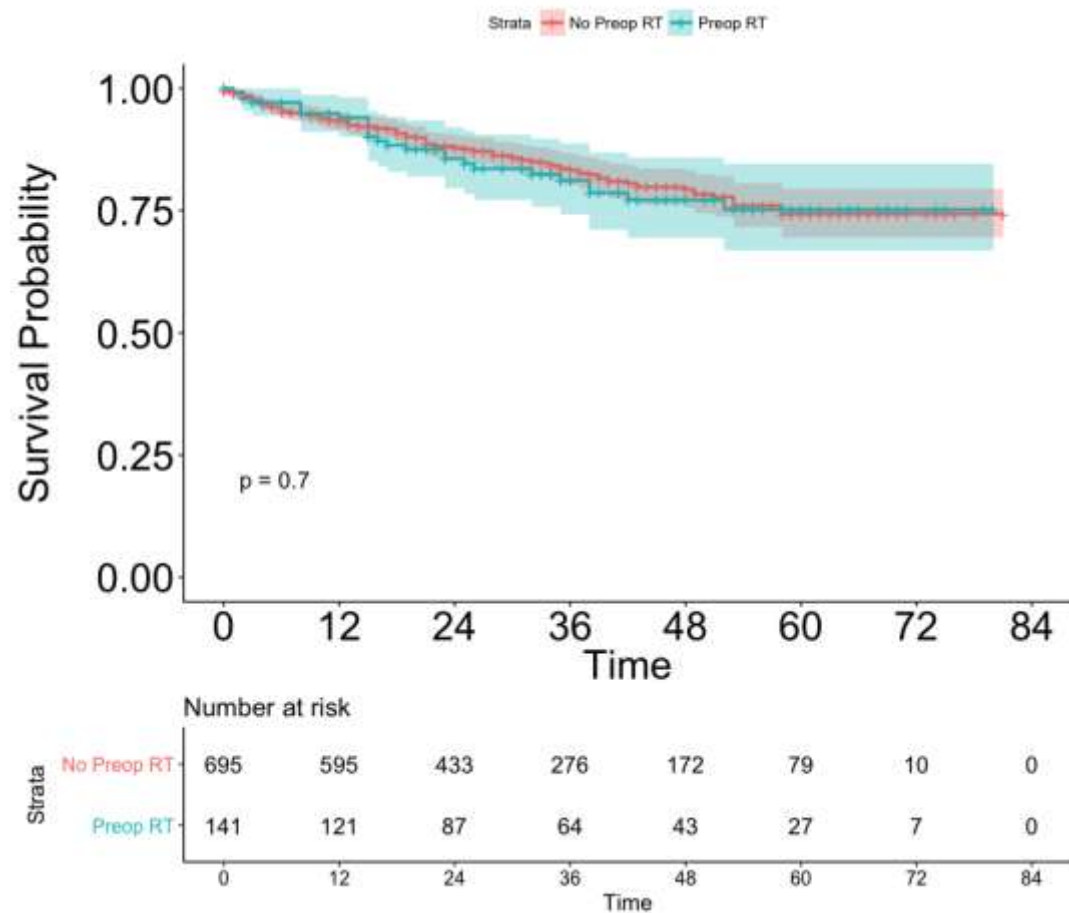
DSS



STREXIT

Survival by Rx -Preop RT

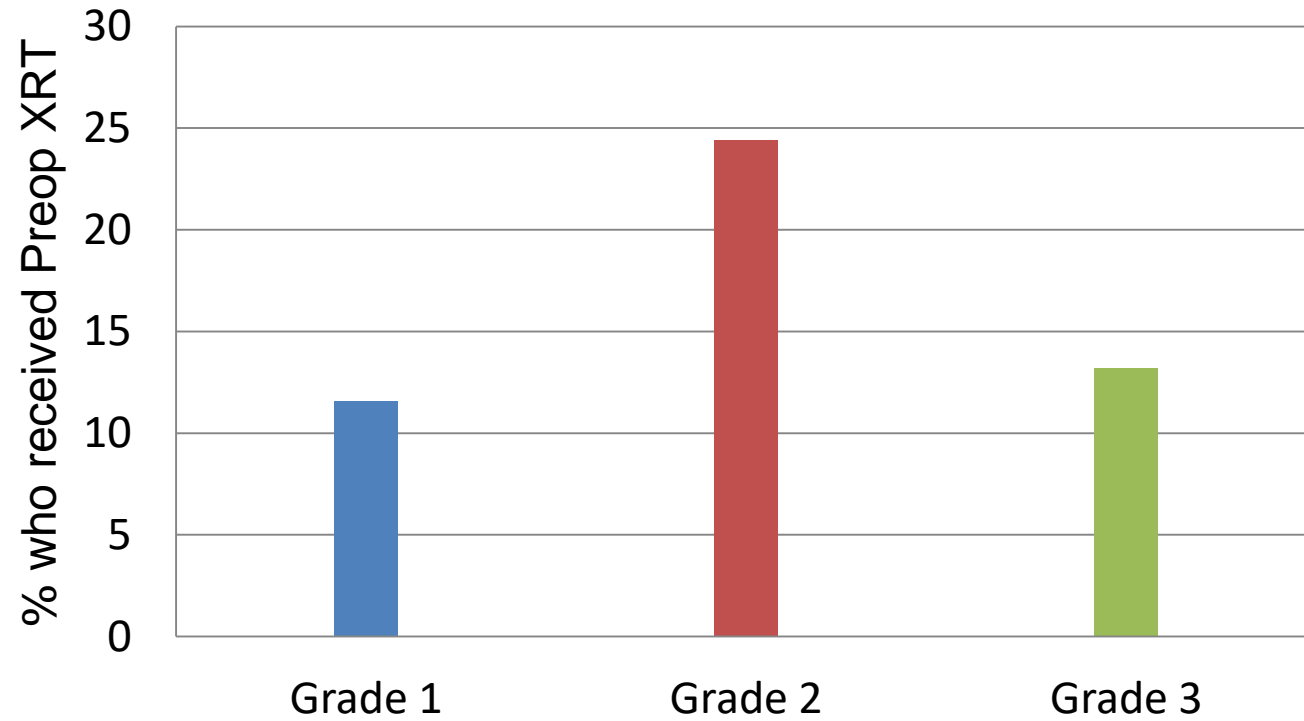
DSS



P val = 0.16

STREXIT

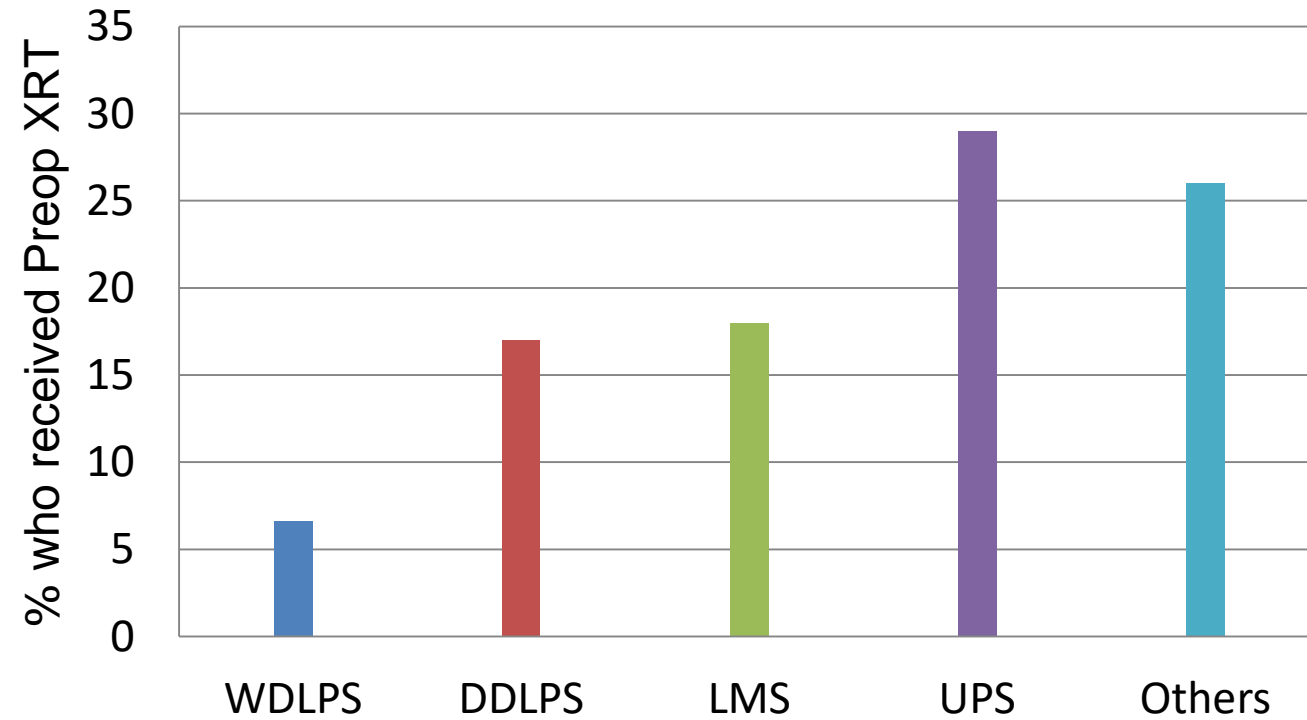
Preop XRT by Grade



For N=836
preop XRT = 16.9%

STREXIT

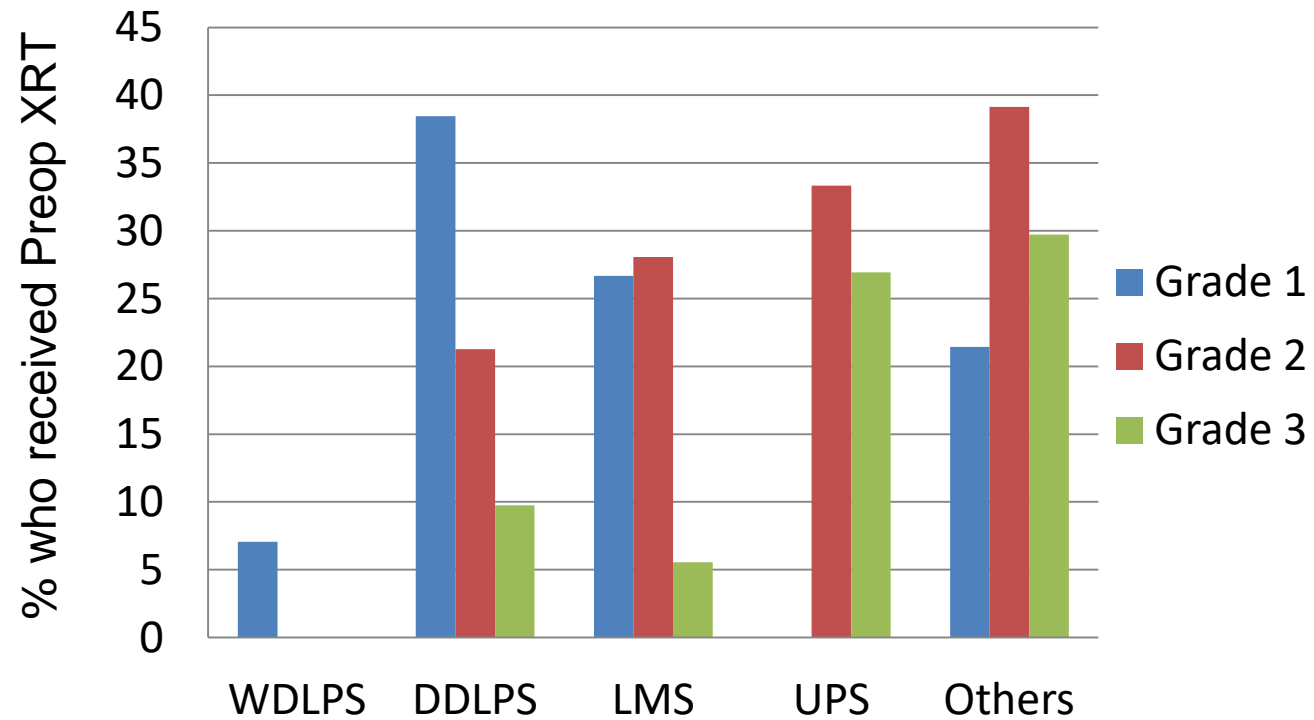
Preop XRT by Histology



For N=836
preop XRT = 16.9%

STREXIT

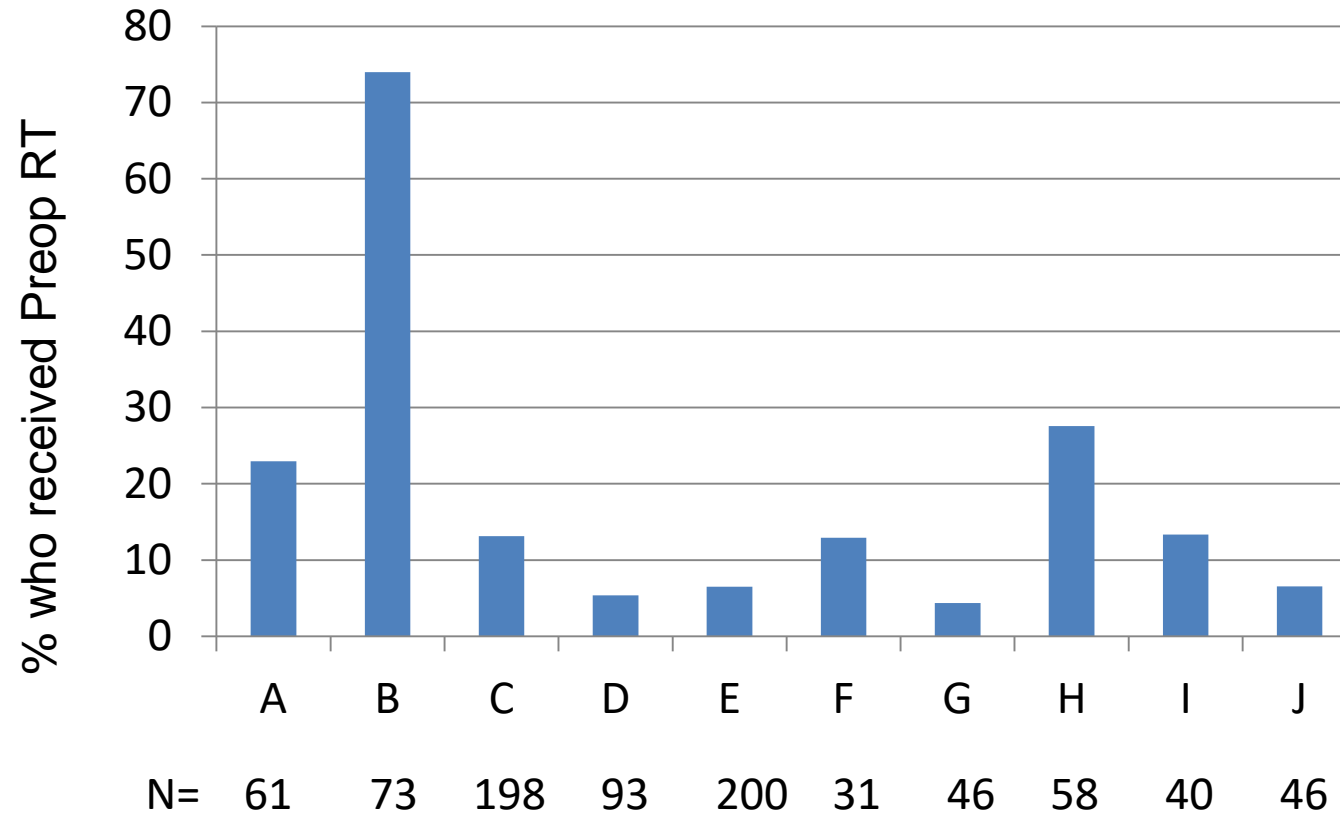
Preop XRT by Histology and Grade



For N=836
preop XRT = 16.9%

STREXIT

Preop RT by Center



For N=836
preop XRT = 16.9%

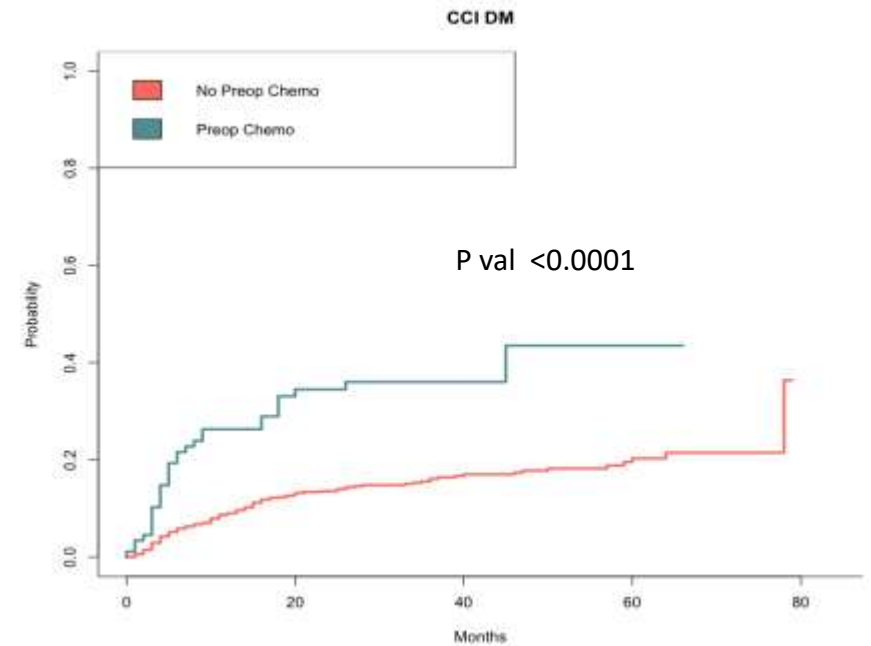
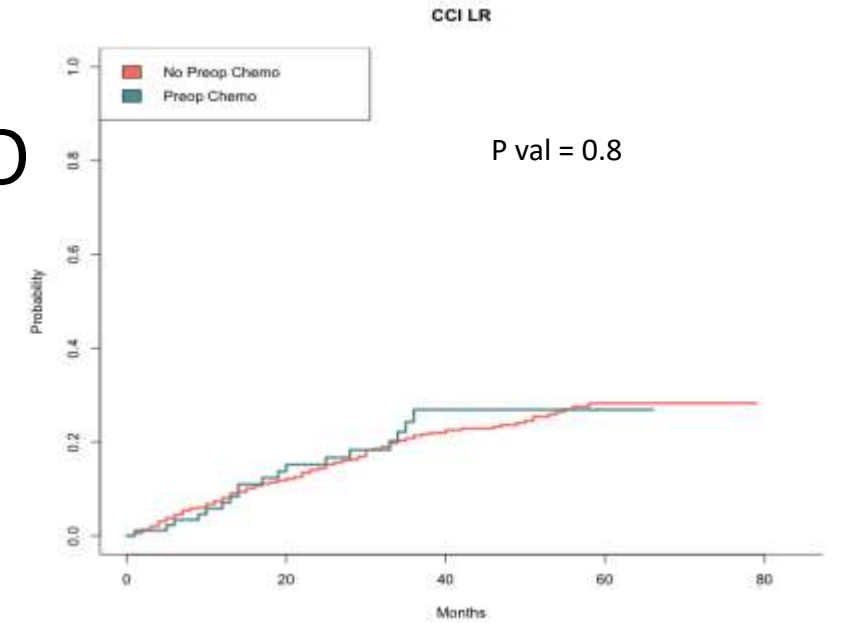
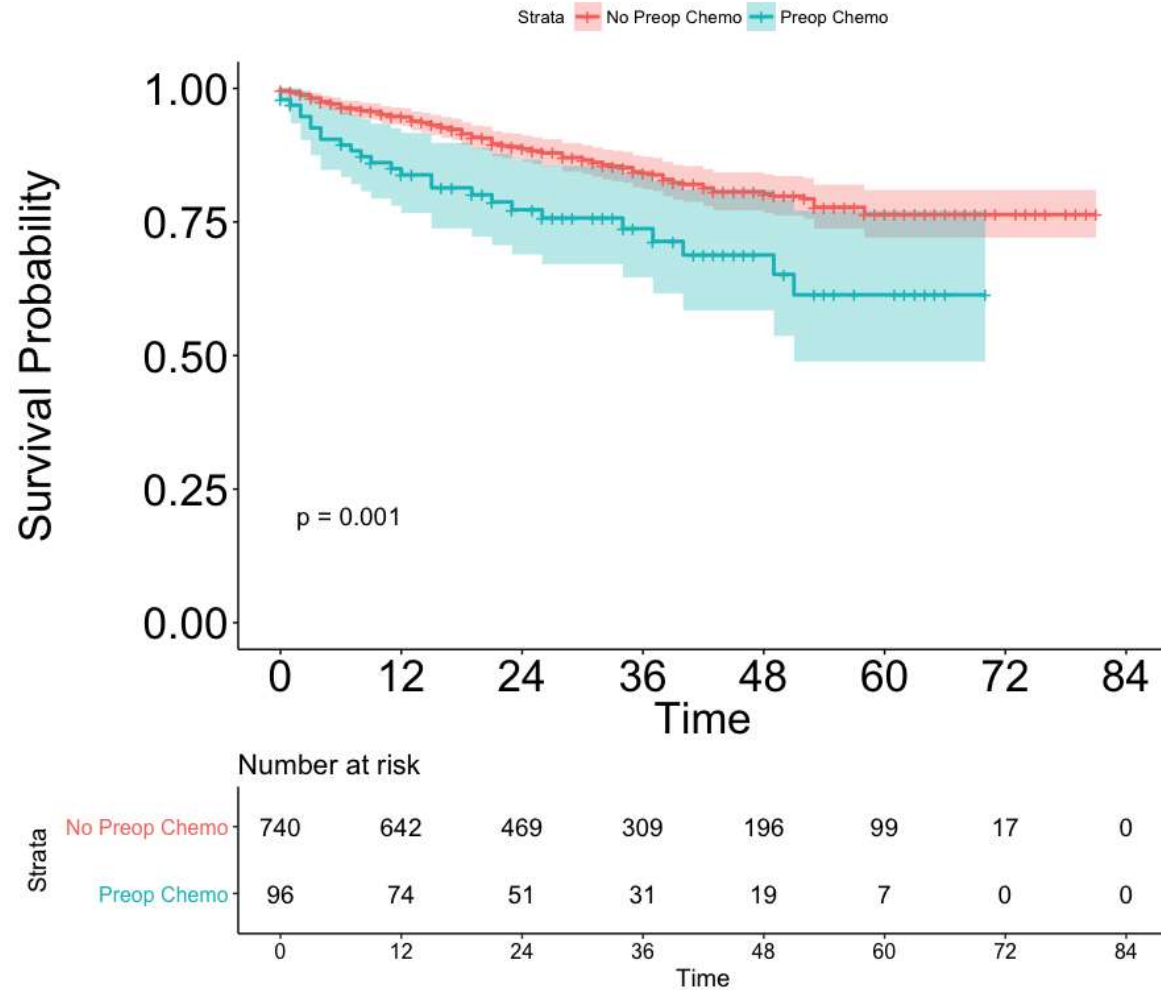
STREXIT

10 centres, prospective data base, ≥ 1 patient on STRASS, 2012-2017

Variation in treatment off trial, by center

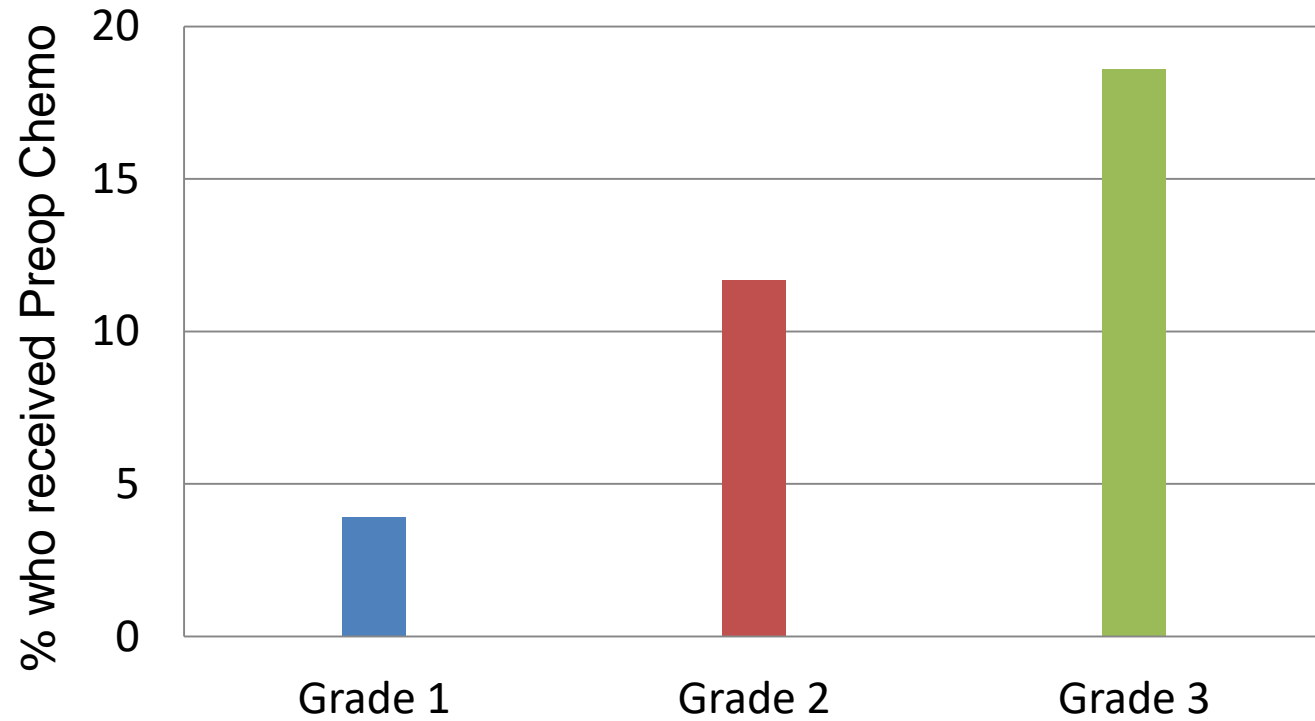
Use of preop RT = 4 - 74%

Survival by Rx -Preop Chemo



STREXIT

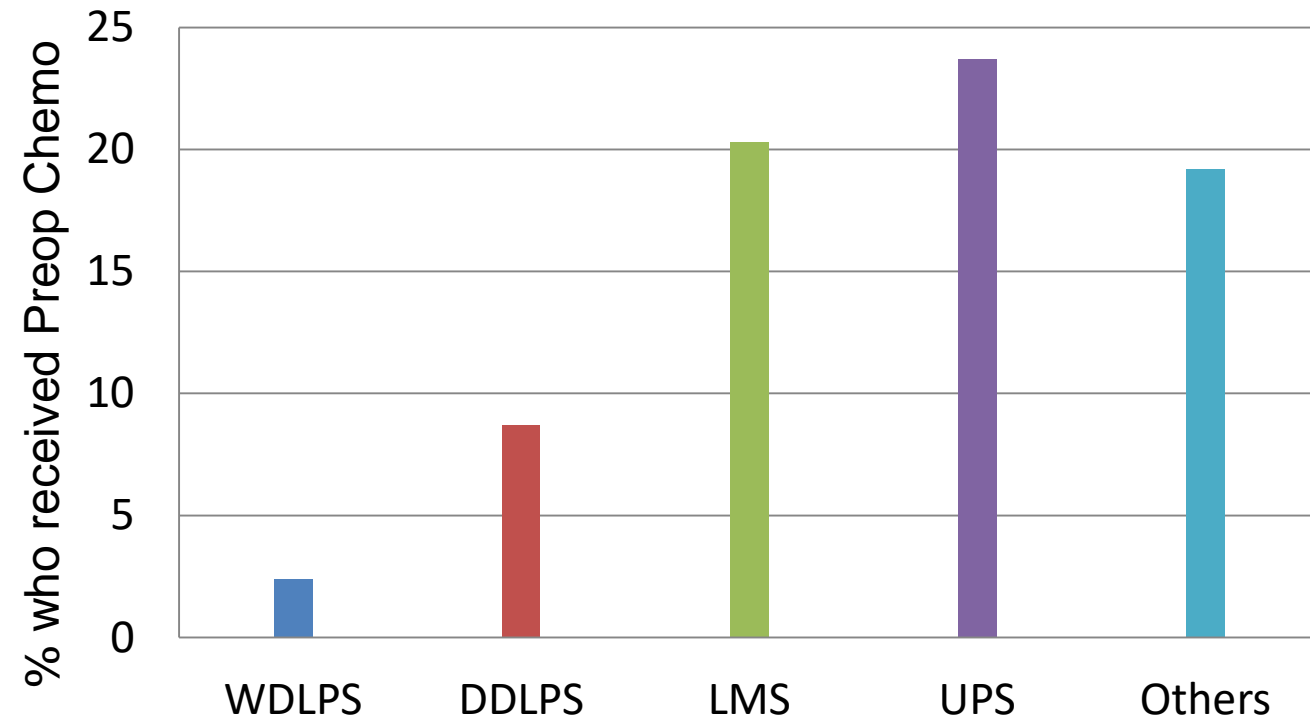
Preop Chemo by Grade



For N=836
preop chemo = 11.5%

STREXIT

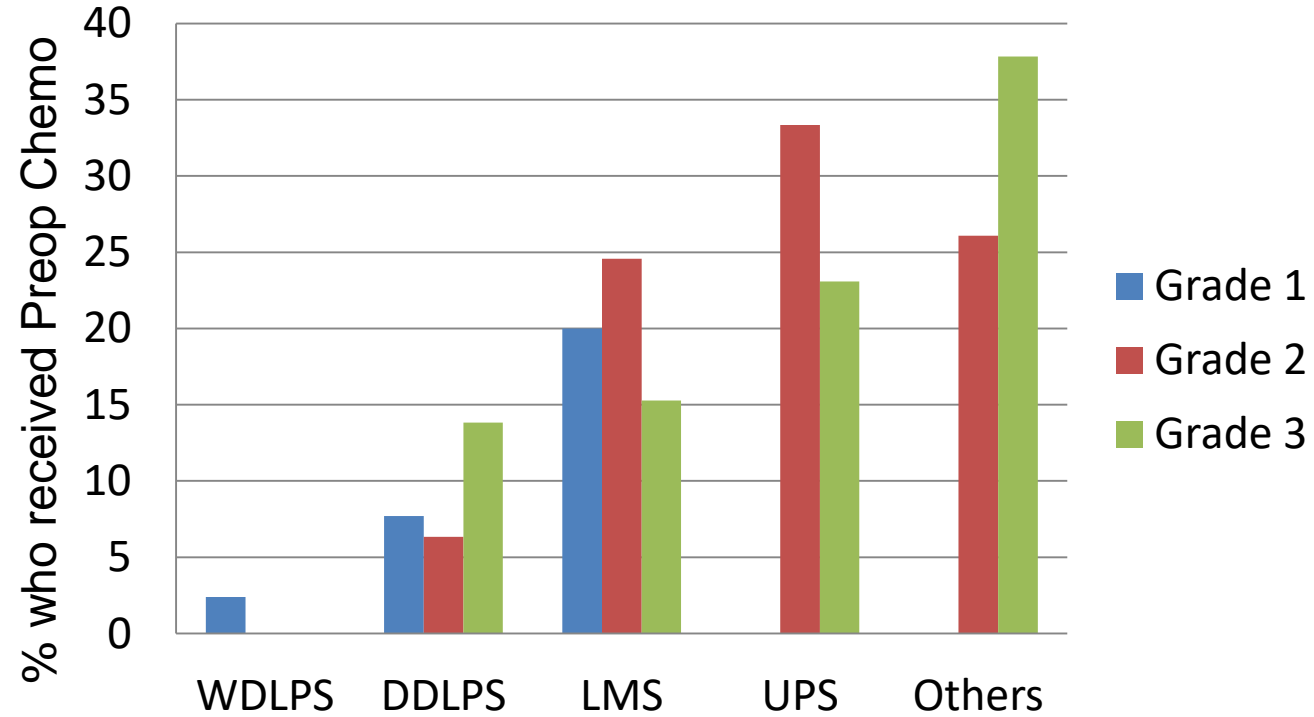
Preop Chemo by Histology



For N=836
preop chemo = 11.5%

STREXIT

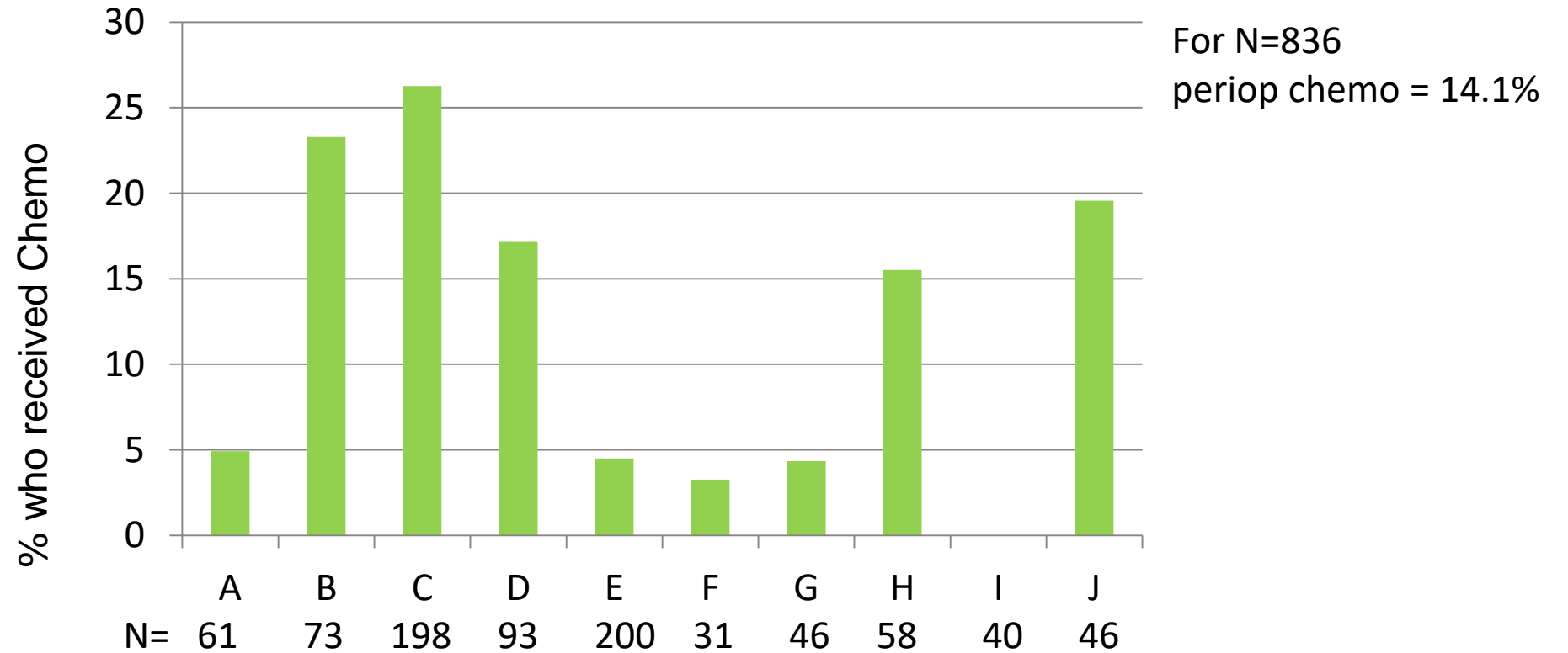
Preop Chemo by Histology and Grade



For N=836
preop chemo = 11.5%

STREXIT

Periop Chemotherapy by Center

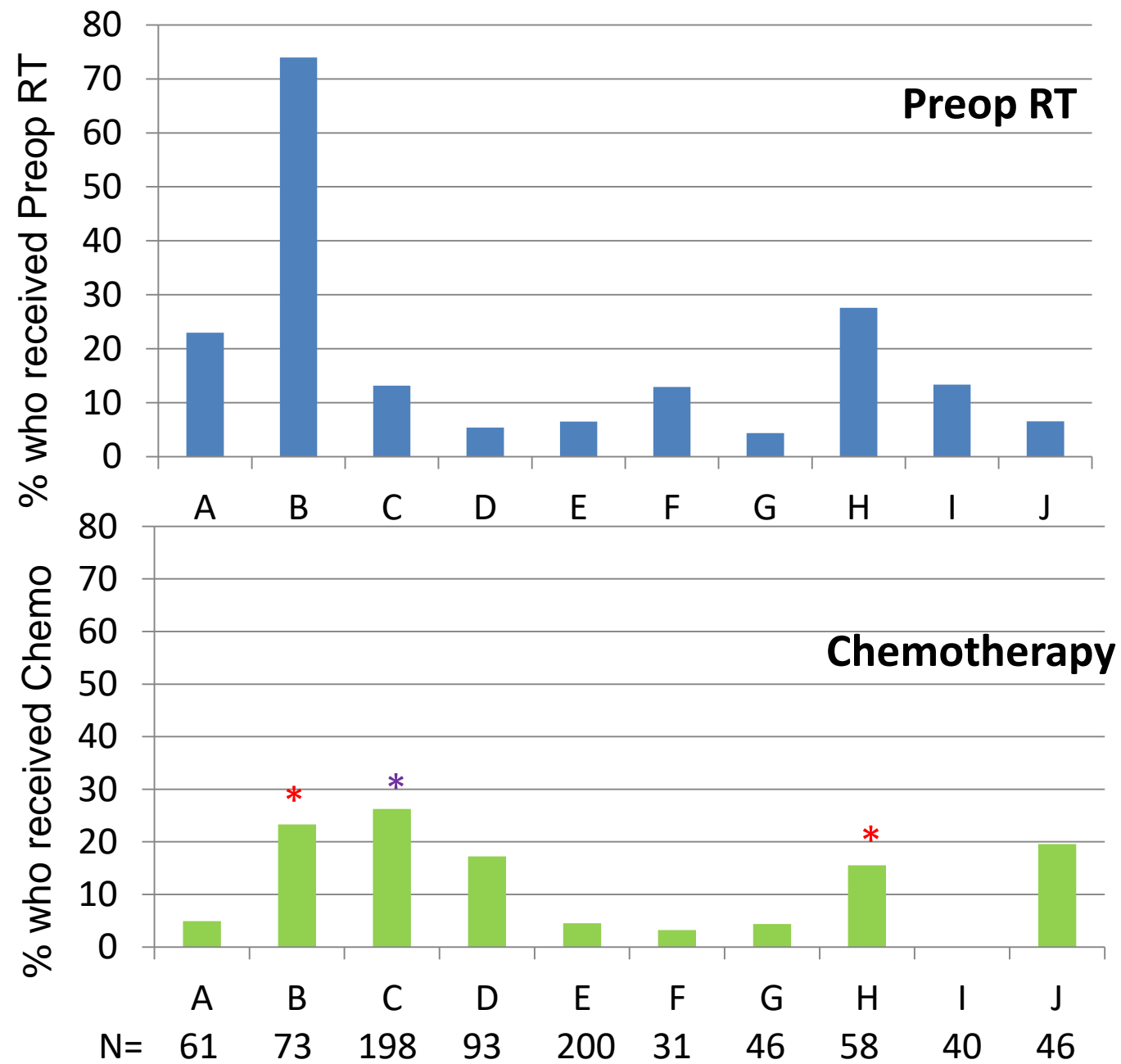


STREXIT

10 centres, prospective data base, ≥ 1 patient on STRASS, 2012-2017

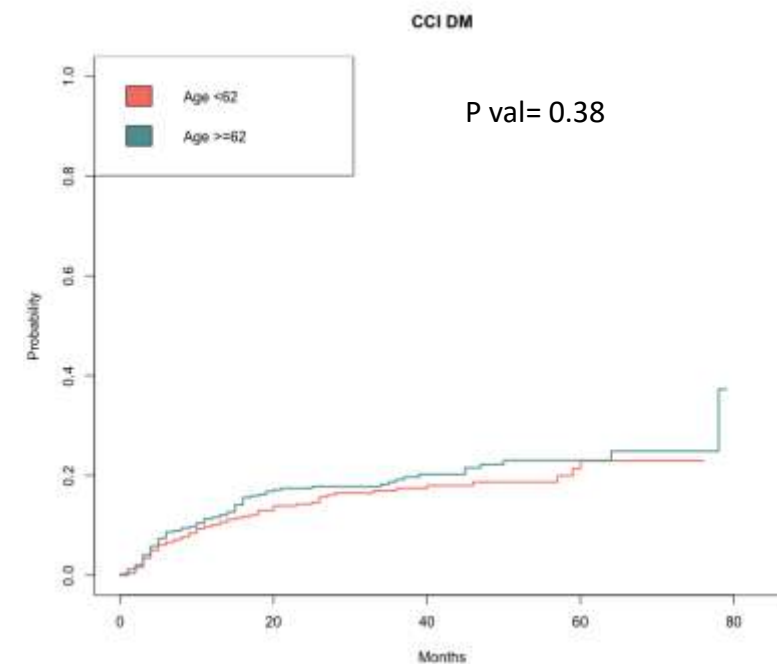
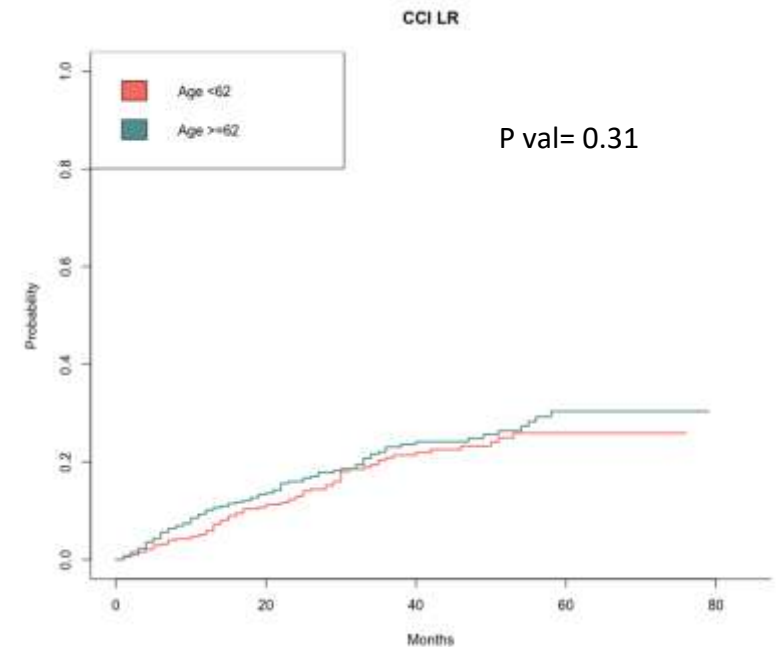
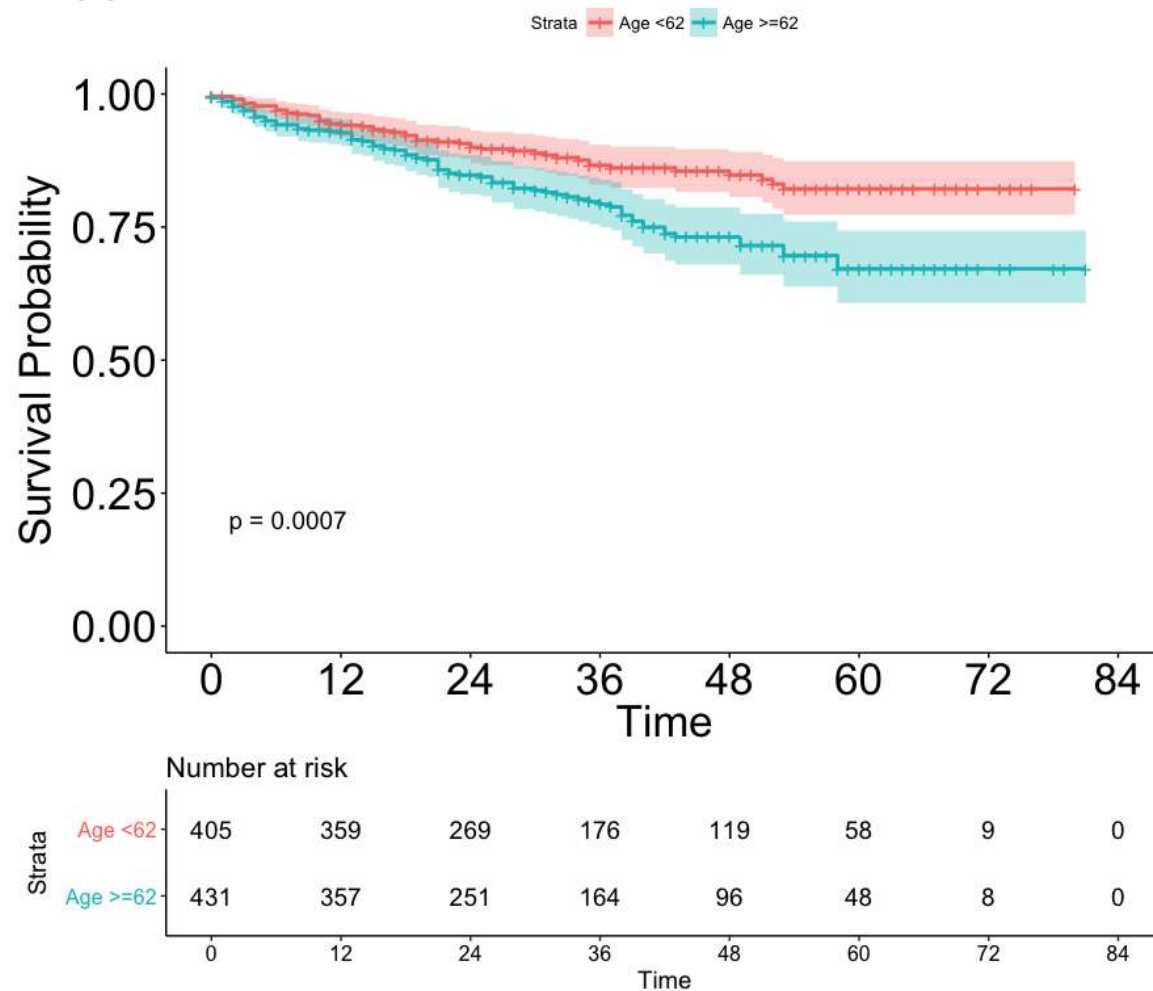
Variation in treatment off trial, by center

Use of peri-op chemo = 0 – 26%



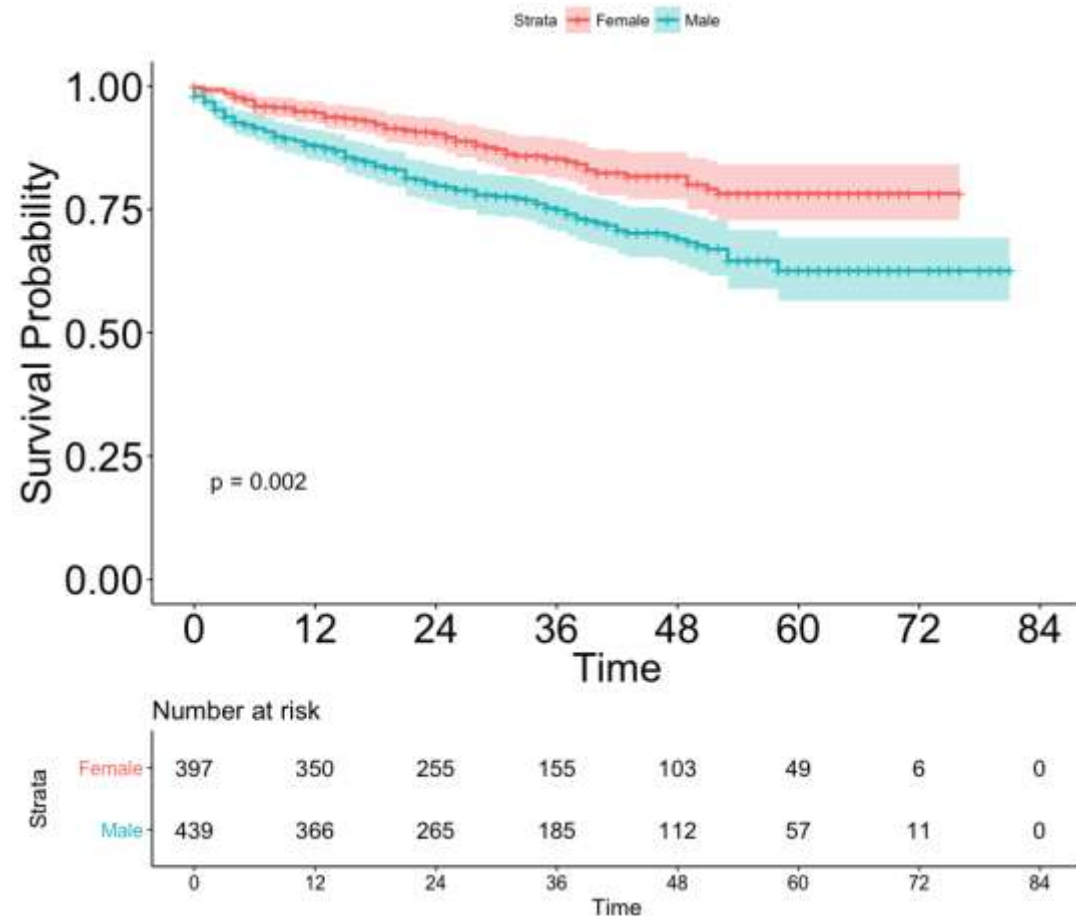
Outcomes by Age

DSS

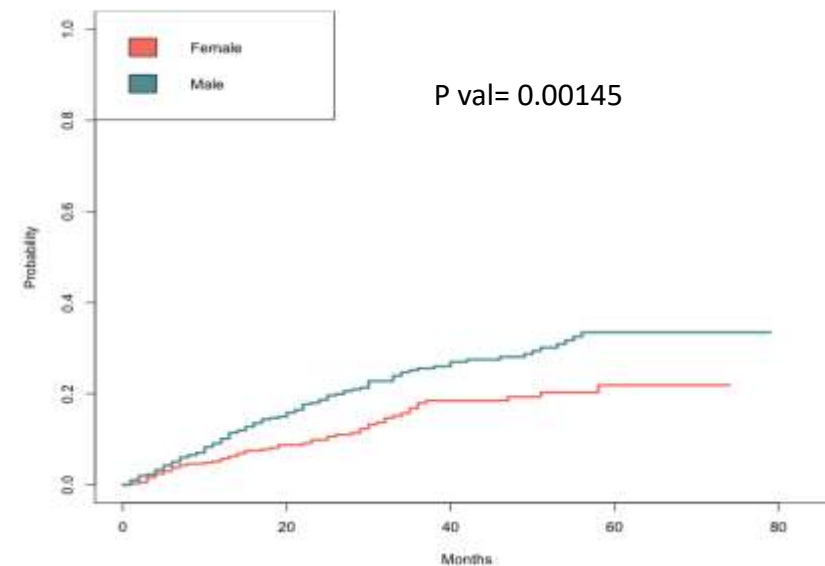


Outcomes by Gender

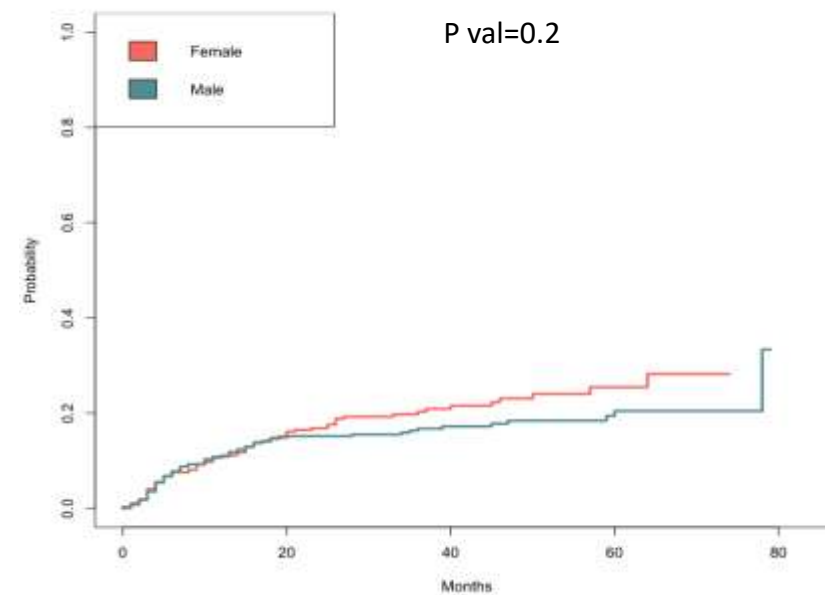
DSS



CCI LR



CCI DM



STREXIT
N= 836

Multivariable Analysis – DS Survival

DSS	HR	95% CI	P val
Age ≥62 vs <62	1.69	1.13 - 2.52	0.01*
Sex Male vs female	2.02	1.38 – 2.95	0.0003*
Tumour size 10-20cm vs <10cm >20cm vs <10cm	1.55 1.80	0.73 – 3.27 0.85 - 3.84	0.08
Completeness of resection R2 vs R0/1	5.31	3.07 - 9.21	<0.0001*
FNCLCC grade II vs I III vs I	1.57 4.82	0.51 – 4.85 1.58 – 14.69	<0.0001*
Histological subtype SFT vs WDLPS LMS vs WDLPS DDLPS vs WDLPS Others vs WDLPS UPS vs WDLPS MPNST vs WDLPS	2.01 3.10 4.14 6.27 4.20 7.08	0.30 – 13.54 0.70 – 13.73 0.98 – 17.44 1.36 – 29.65 0.84 – 20.99 1.24 – 37.24	0.01*
Multifocality Yes vs no	1.03	0.53 – 2.02	0.95
Preoperative RT Yes vs no	1.08	0.69 – 1.70	0.74
Chemotherapy Yes vs no	1.33	0.85 – 2.08	0.21

CONCLUSIONS THUS FAR

STRASS (Ideal World) vs. STREXIT (Real World)

- patient characteristics similar
- tumor size, grade, histologic subtypes differ
- R2 resection rates differ

NEOADJUVANT TRIALS IN RPS

- marked heterogeneity between centers in treatment off study
- multiple interacting biases in offering RCT to patients



STREXIT STUDY: ADVANTAGES

- prospective large scale data
- understanding of selection biases
- international collaborative network



STRASS TRIAL: ADVANTAGES

- genuine prospective data, well curated
- potential tracking of unresected patients
- international collaborative network