

Supplementary table 1. Summary of baseline patient characteristics and initial treatment received for 365 patients with early stage FL.

| | | All Patients | | Stage I | | Stage II | | P value |
|---------------------------|--------------------|--------------|------|------------|------|------------|------|---------|
| | | n = 365 | 100% | n=221 | 61% | n=144 | 39% | |
| Age | Median (Range) | 63 (21-94) | | 61 (21-94) | | 62 (28-85) | | 0.55 |
| Sex | Male | 209/365 | 57.2 | 120/221 | 54.3 | 89/144 | 61.8 | 0.178 |
| ECOG PS | ≥2 | 18/365 | 4.9 | 13/221 | 5.9 | 5/144 | 3.5 | 0.428 |
| B Symptoms | Present | 24/361 | 6.6 | 16/217 | 7.4 | 8/144 | 5.6 | 0.643 |
| LoNoDiam | ≥7cm | 36/271 | 13.3 | 9/161 | 5.6 | 27/110 | 24.5 | <0.001 |
| Nodal Sites | 0 | 40/360 | 11.1 | 40/218 | 18.3 | 0/142 | 0.0 | <0.001 |
| | 1 | 190/360 | 52.8 | 178/218 | 81.7 | 12/142 | 8.4 | |
| | 2 | 111/360 | 30.8 | 0/218 | 0.0 | 111/142 | 78.2 | |
| | 3 | 15/360 | 4.2 | 0/218 | 0.0 | 15/142 | 10.6 | |
| | 4 | 4/360 | 1.1 | 0/218 | 0.0 | 4/142 | 2.8 | |
| Extranodal Sites | Present | 63/362 | 17.4 | 40/220 | 18.2 | 23/142 | 16.2 | 0.776 |
| Grade | 3A | 56/351 | 15.9 | 38/212 | 17.9 | 18/139 | 12.9 | 0.273 |
| B2M | > ULN | 40/182 | 22.0 | 22/111 | 19.8 | 18/71 | 25.3 | 0.463 |
| FLIPI Score | 0 | 111/342 | 32.5 | 80/210 | 38.1 | 31/132 | 23.5 | 0.001 |
| | 1 | 177/342 | 51.8 | 107/210 | 51.0 | 70/132 | 53.0 | |
| | 2 | 50/342 | 14.6 | 23/210 | 10.9 | 27/132 | 20.5 | |
| | 3 | 4/342 | 1.2 | 0/210 | 0.0 | 4/132 | 3.0 | |
| Watch and Wait | Observation | 85/365 | 23.3 | 49/221 | 22.2 | 36/144 | 25.0 | 0.532 |
| Active Treatment | RT Alone | 171/365 | 46.8 | 125/172 | 72.7 | 46/144 | 31.9 | <0.001 |
| | Immunochemotherapy | 63/365 | 17.2 | 21/172 | 12.2 | 42/144 | 29.1 | <0.001 |
| | CMT | 46/365 | 12.6 | 26/172 | 15.1 | 20/144 | 13.9 | 0.412 |
| Maintenance Therapy | | 49/280 | 17.5 | 16/172 | 9.3 | 33/108 | 30.6 | <0.001 |
| Median Follow-up (months) | | 45 | | 48 | | 43 | | 0.505 |

LoNoDiam = Largest nodal diameter; B2M = beta 2 microglobulin; ECOG PS = performance status; ULN = upper limit normal; XRT = radiotherapy; CMT = combined modality therapy

Supplementary table 2. Summary of baseline characteristics among treatment arms for actively treated patients with early stage FL.

| | | RT Alone | | Systemic Therapy (n = 109) | | | | RT vs ICT vs CMT P value | RT vs ICT+CMT p value | ICT vs CMT p value |
|-------------------|----------------|------------------|------|----------------------------|------|---------------------------------|------|-----------------------------|--------------------------|-----------------------|
| | | n=171 | % | Immunochemotherapy (ICT) | | Combined modality therapy (CMT) | | | | |
| | | n=63 | % | n=46 | % | | | | | |
| Age | Median (Range) | 63 (28 – 85) | | 63 (21-88) | | 54 (28-82) | | 0.368 | 0.014 | 0.245 |
| Sex | Male | 95/170 | 55.9 | 36/63 | 57.1 | 28/46 | 60.9 | 0.847 | 0.732 | 0.844 |
| ECOG | >2 | 8/171 | 4.7 | 5/63 | 7.9 | 1/46 | 2.2 | 0.376 | 0.978 | 0.398 |
| B Symptoms | Present | 7/167 | 4.2 | 12/63 | 19.0 | 1/46 | 2.2 | <0.001 | 0.0289 | 0.007 |
| LoNoDiam | >7cm | 9/132 | 6.8 | 13/53 | 24.5 | 8/30 | 26.6 | 0.001 | <0.001 | 0.589 |
| No nodal sites | >2 | 4/170 | 2.4 | 9/62 | 14.5 | 2/44 | 4.5 | 0.002 | <0.001 | 0.115 |
| Extranodal | Extranodal | 29/171 | 16.9 | 9/62 | 14.5 | 6/45 | 13.3 | 0.797 | 0.613 | 0.999 |
| Stage | I | 125/171 | 73.1 | 21/63 | 33.3 | 26/46 | 56.5 | <0.001 | <0.001 | 0.320 |
| Grade | 3A | 26/165 | 15.7 | 11/58 | 18.9 | 8/46 | 17.4 | 0.846 | 0.617 | 0.999 |
| B2M | > ULN | 19/68 | 27.9 | 9/33 | 27.2 | 5/35 | 14.3 | 0.682 | 0.562 | 0.745 |
| FLIPI Score | 0 | 55/161 | 34.2 | 15/60 | 25.0 | 23/44 | 52.2 | 0.029 | 0.159 | 0.014 |
| | 1 | 82/161 | 50.9 | 31/60 | 51.6 | 16/44 | 36.3 | | | |
| | 2 | 24/161 | 14.9 | 12/60 | 20.0 | 4/44 | 9.0 | | | |
| | 3 | 0/161 | 0 | 2/60 | 3.0 | 1/44 | 2.2 | | | |
| ORR | | 164/171 | 95.9 | 61/63 | 96.8 | 44/46 | 95.6 | 0.872 | 0.763 | 0.99 |
| CR | | 122/171 | 71.3 | 47/63 | 74.6 | 35/46 | 76.0 | 0.494 | 0.476 | 0.860 |
| Transformation | | 11/171 | 6.4 | 1/63 | 1.6 | 1/46 | 2.1 | 0.161 | 0.087 | 0.999 |
| 5 Yr PFS (95% CI) | | 67.9 (57.5-76.2) | | 86.1 (72.2-93.4) | | 71.6 (54.0-83.5) | | 0.055 | 0.011 | 0.230 |
| 5 Yr OS (95% CI) | | 93.1 (83.3-97.1) | | 90.8 (74.0-96.9) | | 95.0 (80.3-98.7) | | 0.707 | 0.186 | 0.625 |

LoNoDiam = Largest nodal diameter; B2M = beta 2 microglobulin; ECOG PS = performance status; ULN = upper limit normal; ORR = overall response rate; CR = complete response.

Supplementary table 3. Summary of radiotherapy dose (A) and immunochemotherapy and maintenance rituximab (B) received for first line treatment in early stage FL.

A

| | All Radiation | | RT Alone | | CMT | | p value |
|------------|---------------|------|----------|------|--------|------|---------|
| | n = 187 | % | n = 149 | % | n = 38 | % | |
| <24 Gy | 5/187 | 2.7 | 4/149 | 2.6 | 1/38 | 2.6 | 0.127 |
| 24-30 Gy | 134/187 | 71.7 | 112/149 | 75.2 | 22/38 | 57.9 | |
| 30.1-36 Gy | 42/187 | 22.4 | 28/149 | 18.8 | 14/38 | 36.9 | |
| >36 Gy | 6/187 | 3.2 | 5/149 | 3.4 | 1/38 | 2.6 | |

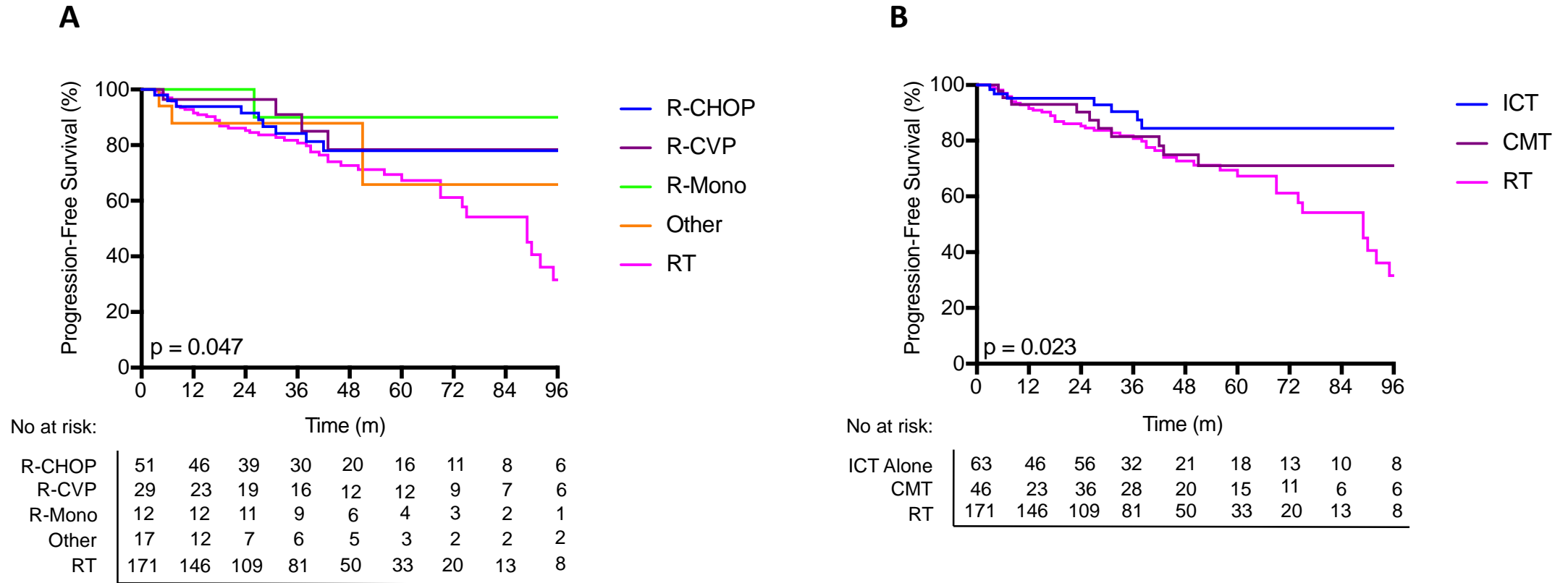
B

| | All Systemic | | Immunochemotherapy | | CMT | | p value |
|-----------------------|--------------|------|--------------------|------|-------|------|---------|
| | n | % | n | % | n | % | |
| R-CHOP | 51/109 | 46.7 | 33/63 | 52.4 | 18/46 | 39.1 | 0.189 |
| R-CVP | 29/109 | 26.6 | 9/63 | 14.3 | 20/46 | 43.5 | 0.0009 |
| BR | 11/109 | 10.1 | 7/63 | 11.1 | 4/46 | 8.7 | 0.7573 |
| Rituximab Monotherapy | 12/109 | 11.1 | 8/63 | 12.7 | 4/46 | 8.7 | 0.7776 |
| Other | 6/109 | 5.5 | 6/63 | 9.5 | 0/46 | 0.0 | 0.0382 |
| Rituximab Maintenance | 49/109 | 45 | 37/63 | 58.7 | 12/46 | 26.1 | 0.0001 |

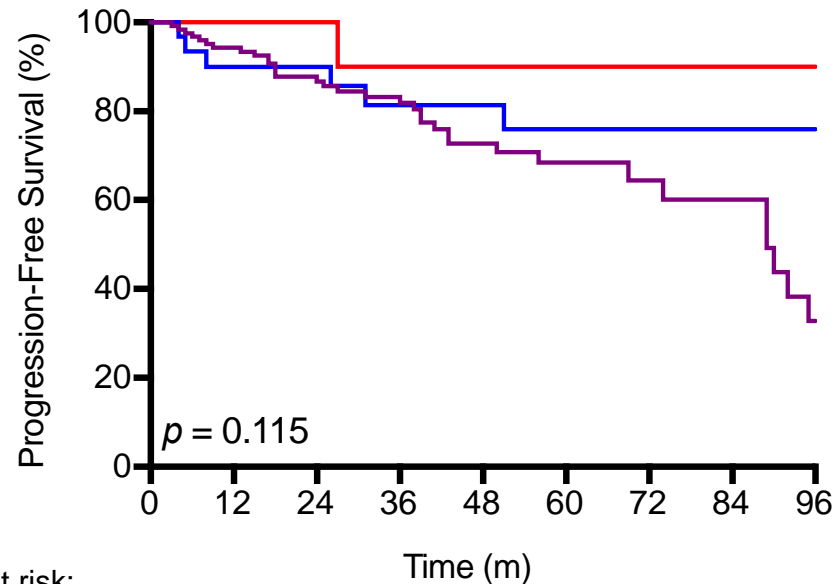
Supplementary table 4. Summary of baseline characteristics among treatment approaches for actively treated patients with early stage FL.

| | | Radiation | | Systemic therapy* | | Systemic + maintenance rituximab | | P value |
|----------------|------------|-----------|------|-------------------|------|----------------------------------|------|---------|
| | | n=171 | % | n=60 | % | n=49 | % | All |
| Age | >60 yrs | 101/170 | 59.4 | 27/60 | 45.0 | 29/48 | 60.4 | 0.128 |
| Sex | Male | 96/170 | 56.4 | 33/60 | 55.0 | 31/49 | 63.3 | 0.627 |
| ECOG | >2 | 8/171 | 4.7 | 3/60 | 5.0 | 3/49 | 6.1 | 0.92 |
| B Symptoms | Present | 7/167 | 4.2 | 4/60 | 6.7 | 9/49 | 18.4 | 0.003 |
| LoNoDiam | >7cm | 9/132 | 6.8 | 6/41 | 14.6 | 15/42 | 35.7 | <0.001 |
| No nodal sites | >2 | 4/170 | 2.4 | 4/60 | 6.7 | 7/47 | 14.9 | 0.003 |
| Extranodal | Extranodal | 29/171 | 17.0 | 7/60 | 11.7 | 8/47 | 17.0 | 0.608 |
| Stage | II | 46/171 | 26.9 | 29/60 | 48.3 | 33/49 | 67.3 | <0.001 |
| Grade | 3A | 26/165 | 15.8 | 13/59 | 22.0 | 6/45 | 13.3 | 0.433 |
| B2M | > ULN | 19/68 | 27.9 | 7/41 | 17.1 | 7/28 | 25.0 | 0.434 |
| Hb, g/dL | <12 | 11/169 | 6.5 | 4/59 | 6.8 | 9/49 | 18.4 | 0.029 |
| LDH | >ULN | 24/162 | 14.8 | 8/58 | 13.8 | 13/49 | 26.5 | 0.125 |
| FLIPI | Low Risk | 24/161 | 14.9 | 7/58 | 12.1 | 12/46 | 26.1 | 0.12 |

*Systemic therapy includes immunochemotherapy and CMT.

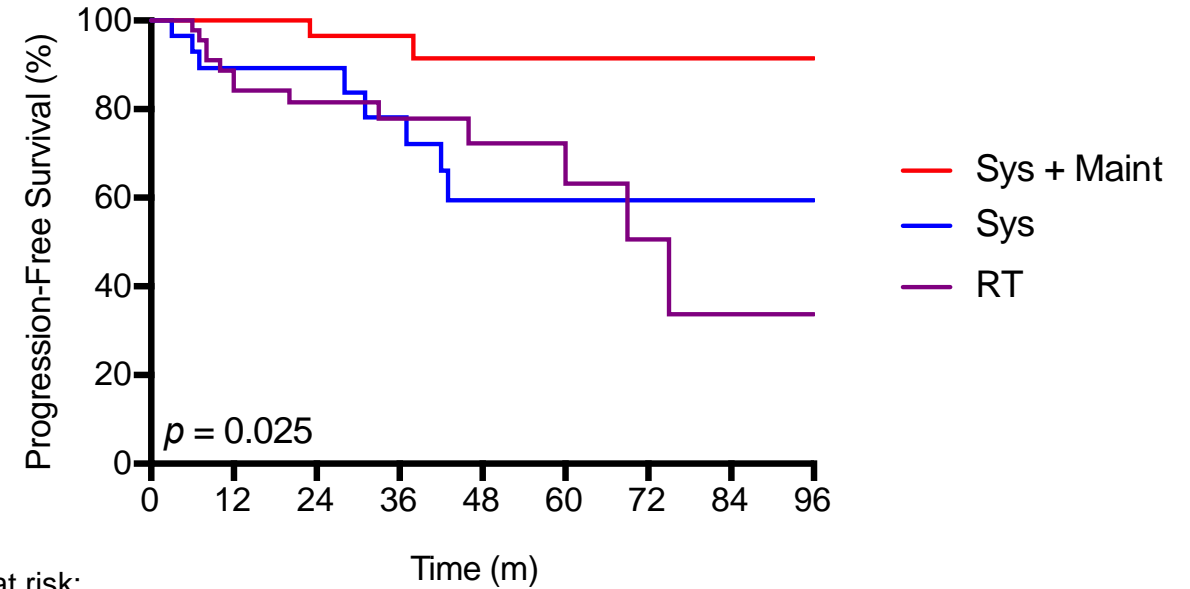


Supplementary Figure 1. A) Progression-free survival among patients treated with different chemotherapy regimens or radiotherapy (RT). Comparing chemotherapy regimens only demonstrated no significant difference in PFS ($P=0.722$). Other: $n=11$ Bendamustine-rituximab, $n=4$ chlorambucil-rituximab, $n=2$ cyclophosphamide, prednisone, rituximab. B) Progression-free survival among patients treated with RT, combined modality therapy (CMT) and immunochemotherapy (ICT). Comparing ICT vs CMT vs RT demonstrated a significant difference in PFS ($P=0.023$). Comparing CMT vs ICT demonstrated no significant difference in PFS ($P=0.24$).

A

No at risk:

| | | | | | | | | | |
|-------------|-----|-----|----|----|----|----|----|----|---|
| RT | 124 | 112 | 81 | 62 | 40 | 26 | 17 | 12 | 7 |
| Sys | 31 | 24 | 22 | 19 | 16 | 14 | 9 | 7 | 6 |
| Sys + Maint | 16 | 16 | 11 | 9 | 6 | 5 | 3 | 3 | 2 |

B

No at risk:

| | | | | | | | | | |
|-------------|----|----|----|----|----|---|---|---|---|
| RT | 46 | 39 | 29 | 20 | 21 | 8 | 4 | 2 | 2 |
| Sys | 29 | 23 | 17 | 14 | 9 | 7 | 5 | 3 | 3 |
| Sys + Maint | 33 | 32 | 27 | 21 | 12 | 9 | 8 | 5 | 5 |

Supplementary Figure 2. Progression-free survival for stage I (A) and stage II (B) patients treated with radiotherapy alone, systemic therapy without maintenance rituximab and systemic therapy with maintenance rituximab.