

Table S1: Immunosuppression practice variability among centers at years 1, 3 and 5 post-LT according to center LT volume

Percent of recipients on regimen by center at Year 1			
	Low volume (<75 th %ile)* (n=69 centers)	High volume (≥75 th %ile)* (n=29 centers)	p-value
CNI monotherapy			0.232
<i>Median</i>	49.6	56.2	
<i>IQR</i>	37.5-62.2	37.9-64.5	
<i>Range</i>	20.0-77.5	27.1-79.7	
CNI + antiM			0.421
<i>Median</i>	22.9	19.5	
<i>IQR</i>	13.7-29.3	12.4-26.5	
<i>Range</i>	2.7-52.9	7.3-52.2	
CNI + steroid			0.935
<i>Median</i>	5.9	5.6	
<i>IQR</i>	3.1-8.9	4.0-8.0	
<i>Range</i>	1.0-35.0	1.7-30.9	
CNI + antiM + steroid			0.038
<i>Median</i>	4.8	2.9	
<i>IQR</i>	2.7-8.8	2.2-6.0	
<i>Range</i>	0-31.7	0-22.0	
mTORi-based			0.828
<i>Median</i>	7.8	7.8	
<i>IQR</i>	5.4-13.0	5.0-13.2	
<i>Range</i>	0-38.8	0.1-34.9	
Percent of recipients on regimen by center at Year 3			
	Low volume (<75 th %ile)* (n=63 centers)	High volume (≥75 th %ile)* (n=29 centers)	p-value
CNI monotherapy			0.883
<i>Median</i>	69.3	67.7	
<i>IQR</i>	53.8-74.0	55.6-76.9	
<i>Range</i>	24.5-100.0	37.1-85.4	
CNI + antiM			0.788
<i>Median</i>	13.2	13.9	
<i>IQR</i>	7.9-20.8	9.5-16.9	
<i>Range</i>	0-47.3	2.8-37.7	
CNI + steroid			0.880
<i>Median</i>	4.2	4.2	
<i>IQR</i>	2.5-7.1	2.8-6.3	
<i>Range</i>	0-19.6	0-17.1	
CNI + antiM + steroid			0.634
<i>Median</i>	2.2	2.1	
<i>IQR</i>	0-4.1	1.0-4.1	
<i>Range</i>	0-18.9	0-13.5	
mTORi-based			0.665
<i>Median</i>	7.5	7.1	
<i>IQR</i>	3.4-10.7	4.3-12.0	

<i>Range</i>	0-36.4	0-38.5	
Percent of recipients on regimen by center at Year 5			
	Low volume (<75 th %ile)* (n=53 centers)	High volume (≥75 th %ile)* (n=29 centers)	p-value
CNI monotherapy			0.687
<i>Median</i>	70.0	70.4	
<i>IQR</i>	57.7-78.3	62.9-77.5	
<i>Range</i>	15.4-95.2	43.0-87.4	
CNI + antiM			0.656
<i>Median</i>	12.8	11.9	
<i>IQR</i>	7.7-19.0	8.3-14.7	
<i>Range</i>	0-35.5	0.9-39.3	
CNI + steroid			0.225
<i>Median</i>	3.3	4.5	
<i>IQR</i>	2.1-5.6	2.5-6.7	
<i>Range</i>	0-15.4	0.9-15.9	
CNI + antiM + steroid			0.512
<i>Median</i>	3.0	2.1	
<i>IQR</i>	0-6.1	0.9-3.7	
<i>Range</i>	0-20.5	0-11.8	
mTORi-based			0.915
<i>Median</i>	6.3	6.1	
<i>IQR</i>	2.3-9.4	2.6-8.7	
<i>Range</i>	0-29.6	0-26.7	

Note: restricted to centers contributing ≥20 recipients to the UNOS-Medicare cohort at each time point to avoid extreme values

*75th %ile equates to an average of 82 LTs per year

Table S2: Mixed-effects logistic regression model evaluating predictors of immunosuppression escalation between years 1 and 3 post-LT (N=7,510)

	aOR (95% CI)	p-value
Female	1.09 (0.88-1.34)	0.440
Age at LT, per 5 years	0.95 (0.90-1.01)	0.082
Race/ethnicity		0.142
White	Reference	
Black	1.43 (1.03-1.99)	
Hispanic	0.98 (0.73-1.30)	
Asian	0.70 (0.39-1.26)	
Other	0.83 (0.33-2.09)	
Liver disease etiology		0.493
Viral	Reference	
ALD	1.00 (0.73-1.35)	
NASH	0.99 (0.74-1.32)	
AI disease*	1.32 (0.96-1.82)	
Other	1.00 (0.71-1.41)	
Pre-LT HCC	1.02 (0.79-1.31)	0.976
Bilirubin at LT, per 1mg/dL	1.00 (0.99-1.01)	0.907
Creatinine at LT, per 1mg/dL	1.12 (1.01-1.26)	0.039
INR, per 1 unit	0.91 (0.79-1.06)	0.241
Pre-LT diabetes	1.02 (0.82-1.27)	0.862
Induction		0.288
None	Reference	
NDI	1.04 (0.80-1.36)	
DI	0.75 (0.51-1.09)	
Rejection in first year	1.28 (0.95-1.71)	0.103
Era		<0.001
2007-2011	Reference	
2012-2016	0.62 (0.51-0.76)	

Table S3: Mixed-effects logistic regression model evaluating predictors of mTORi-based therapy at 1-year post-LT (N=10,219)

	aOR (95% CI)	p-value
Female	0.92 (0.79-1.07)	0.285
Age at LT, per 5 years	1.06 (1.02-1.11)	0.006
Race/ethnicity		0.116
White	Reference	
Black	0.80 (0.61-1.05)	
Hispanic	0.77 (0.62-0.96)	
Asian	0.99 (0.70-1.40)	
Other	1.01 (0.56-1.84)	
Liver disease etiology		0.128
Viral	Reference	
ALD	1.17 (0.96-1.43)	
NASH	1.06 (0.87-1.29)	
AI disease*	0.84 (0.64-1.10)	
Other	1.21 (0.95-1.54)	
Pre-LT HCC	1.51 (1.28-1.79)	<0.001
Bilirubin at LT, per 1mg/dL	1.00 (0.99-1.01)	0.350
Creatinine at LT, per 1mg/dL	1.21 (1.12-1.32)	<0.001
INR, per 1 unit	0.94 (0.84-1.05)	0.256
Pre-LT diabetes	1.11 (0.96-1.29)	0.173
Induction		0.642
None	Reference	
NDI	1.06 (0.86-1.31)	
DI	1.13 (0.85-1.52)	
Rejection in first year	1.30 (1.04-1.63)	0.020
Era		0.090
2007-2011	Reference	
2012-2016	1.13 (0.98-1.30)	

Table S4: Association between maintenance immunosuppression regimen and patient and graft survival stratified by age group

	Patient survival Covariate-adjusted* HR (95% CI)	p-value	Graft survival Covariate-adjusted* HR (95% CI)	p-value
Age at LT <50 (N=1,257)		0.001		<0.001
CNI alone	Reference		Reference	
CNI+antiM	0.83 (0.57-1.22)		0.82 (0.57-1.18)	
CNI+steroid	2.17 (1.45-3.23)		2.27 (1.57-3.28)	
CNI+antiM+steroid	0.92 (0.45-1.91)		1.49 (0.86-2.55)	
mTORi-based	1.45 (0.91-2.33)		1.38 (0.87-2.19)	
Age at LT 50-64 (N=5,034)		<0.001		<0.001
CNI alone	Reference		Reference	
CNI+antiM	0.60 (0.48-0.74)		0.63 (0.51-0.78)	
CNI+ steroid	1.76 (1.37-2.26)		1.82 (1.42-2.32)	
CNI+antiM+steroid	1.20 (0.81-1.79)		1.43 (1.00-2.05)	
mTORi-based	1.50 (1.23-1.83)		1.55 (1.28-1.88)	
Age at LT ≥65 (N=4,125)		<0.001		<0.001
CNI alone	Reference		Reference	
CNI+antiM	0.52 (0.49-0.67)		0.53 (0.41-0.69)	
CNI+ steroid	1.61 (1.21-2.16)		1.60 (1.20-2.14)	
CNI+antiM+steroid	1.10 (0.70-1.75)		1.10 (0.69-1.74)	
mTORi-based	1.34 (1.09-1.65)		1.35 (1.09-1.66)	

* Models adjusted for: sex, race/ethnicity, liver disease diagnosis, pre-LT HCC, bilirubin at LT, creatinine at LT, INR at LT, pre-LT diabetes, induction regimen, acute rejection during year 1, transplant; p-value for interaction of age and regimen was 0.109 in patient survival model and 0.010 in graft survival model; distribution of liver disease diagnoses by age are shown in Supplemental Table 4

Table S5: Distribution of liver transplant indications by age group

	Age <50 years (n=1,365)	Age 50-64 years (n=5,464)	Age ≥65 years (n=4,497)	p-value
Diagnosis				<0.001
Viral hepatitis	39.6%	57.6%	30.6%	
Alcohol	18.5%	13.4%	16.1%	
NASH	11.2%	15.3%	30.2%	
Autoimmune	18.5%	6.3%	11.9%	
Other	12.2%	7.3%	11.2%	

Table S6: Number of creatinine values available in UNOS follow-up data over first 5-years post-LT

Number of creatinine values available in UNOS	Percent of patients between LT-1yr post-LT*	Percent of patients between 1-2yrs post-LT*	Percent of patients between 2-3yrs post-LT*	Percent of patients between 3-4yrs post-LT*	Percent of patients between 4-5yrs post-LT*
0	0.2%	15.1%	17.1%	18.8%	18.9%
1	51.5%	61.5%	63.9%	63.6%	64.8%
2	48.0%	23.3%	19.0%	17.3%	16.2%
≥3	0.3%	0.2%	0.2%	0.2%	0.0%

*Among patients alive with native allograft

Table S7: eGFR by regimen over the first 3-years post-LT

Regimen at 1-year	eGFR Y1* Median (IQR)	p-value	eGFR Y2† Median (IQR)	p-value	eGFR Y3‡ Median (IQR)	p-value
CNI alone	60.8 (48.2-75.6)	<0.001	59.8 (47.0-74.4)	<0.001	58.3 (45.3-72.4)	<0.001
CNI+antiM	59.7 (46.3-75.0)		58.9 (45.5-74.9)		58.4 (44.9-72.9)	
CNI+steroid	57.8 (45.0-76.0)		56.4 (43.0-72.8)		57.8 (43.8-73.6)	
CNI+antiM+steroid	59.5 (49.1-75.0)		59.2 (45.9-73.1)		56.5 (42.9-71.6)	
mTORi-based	54.2 (42.0-72.2)		54.0 (40.2-72.9)		52.5 (39.1-70.2)	
Other	55.8 (43.7-73.0)		58.2 (43.4-70.3)		56.0 (40.1-68.2)	

*Measured between LT and year 1; creatinine values were averaged for patients with >1 creatinine value available during measurement period

†Measured between year 1 and year 2; creatinine values were averaged for patients with >1 creatinine value available during measurement period

‡Measured between year 2 and year 3; creatinine values were averaged for patients with >1 creatinine value available during measurement period

N=66,175 LT recipients in the U.S.
between 1/1/2007-12/31/2016

Excluded N=13,922 (21.0%)

- Age <18 at LT
- Multi-organ recipients
- Prior solid organ recipients

52,253 first LT alone
adult recipients

**Merged with Medicare Master Beneficiary Summary file
and Part A/B claim files**

Excluded N=28,151 (53.9%)

- No Medicare A or B coverage at LT
- No immunosuppression drug claims in either Part D,
Outpatient, Carrier, or DME claim files

24,102 recipients with Medicare A/B at LT
and ≥ 1 immunosuppression drug claim
ever post-LT

Excluded N=12,463 (51.7%)

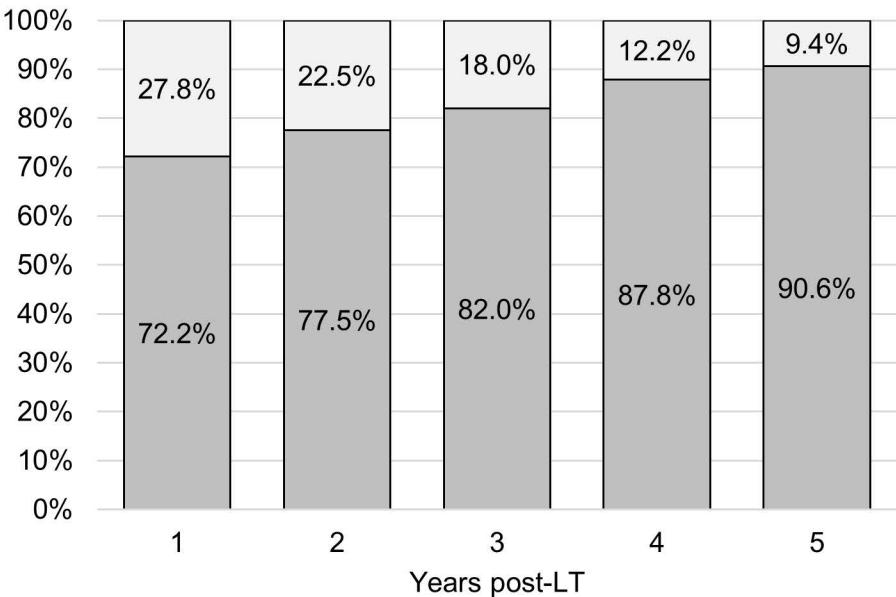
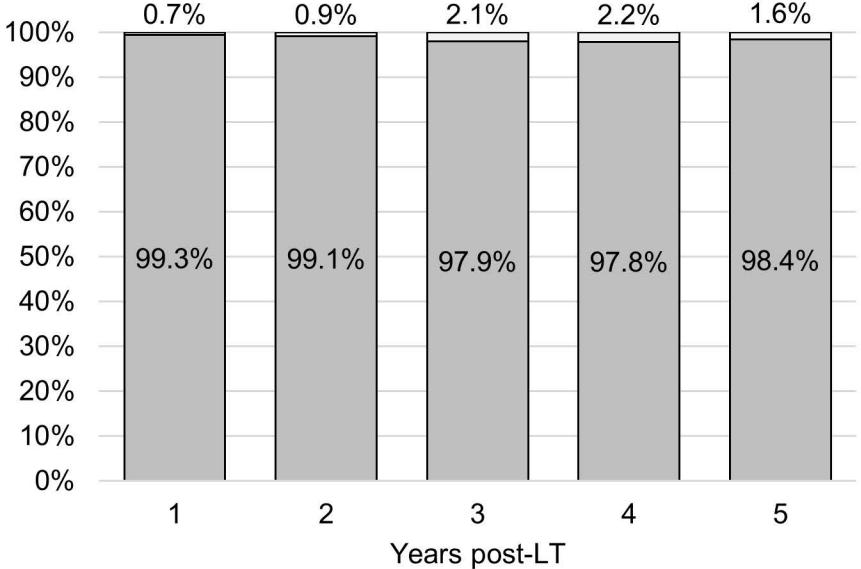
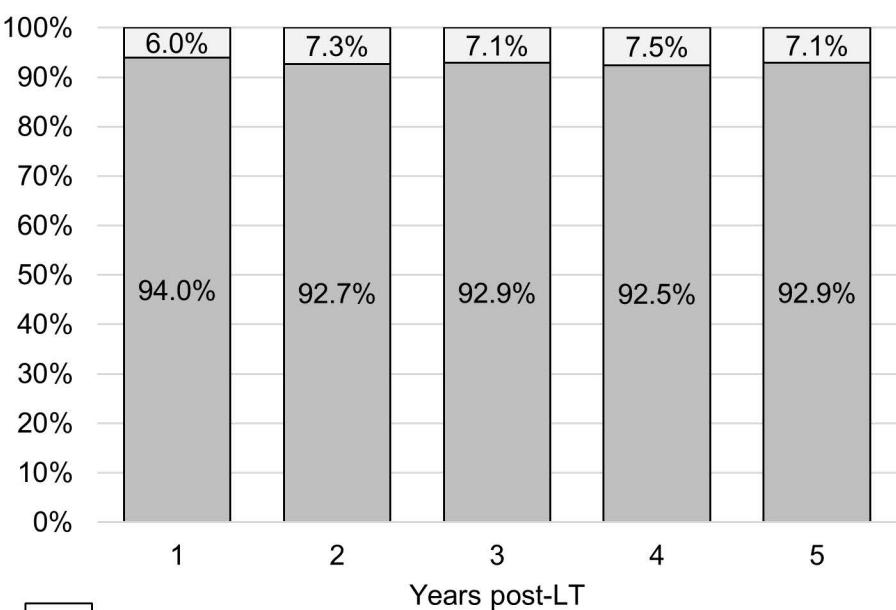
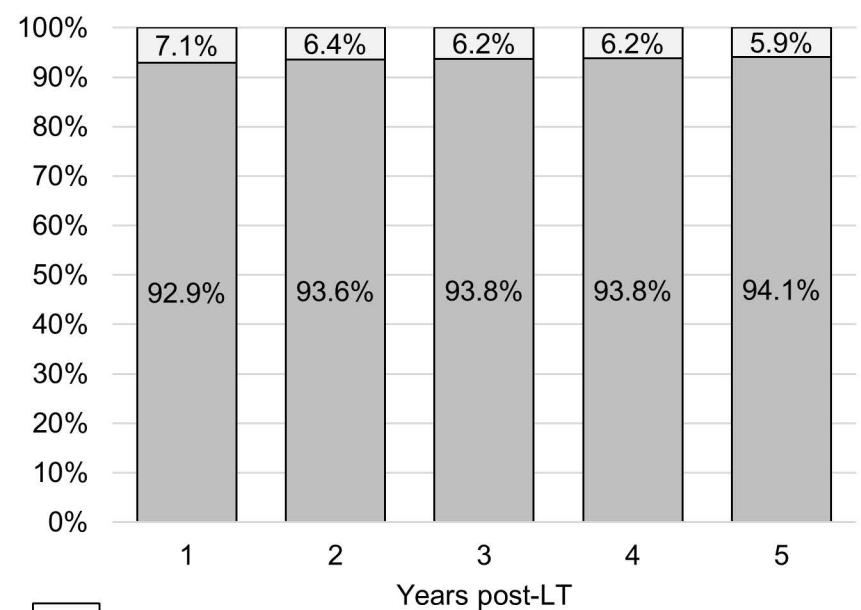
- First non-steroid immunosuppression drug claim >90 days
from LT date

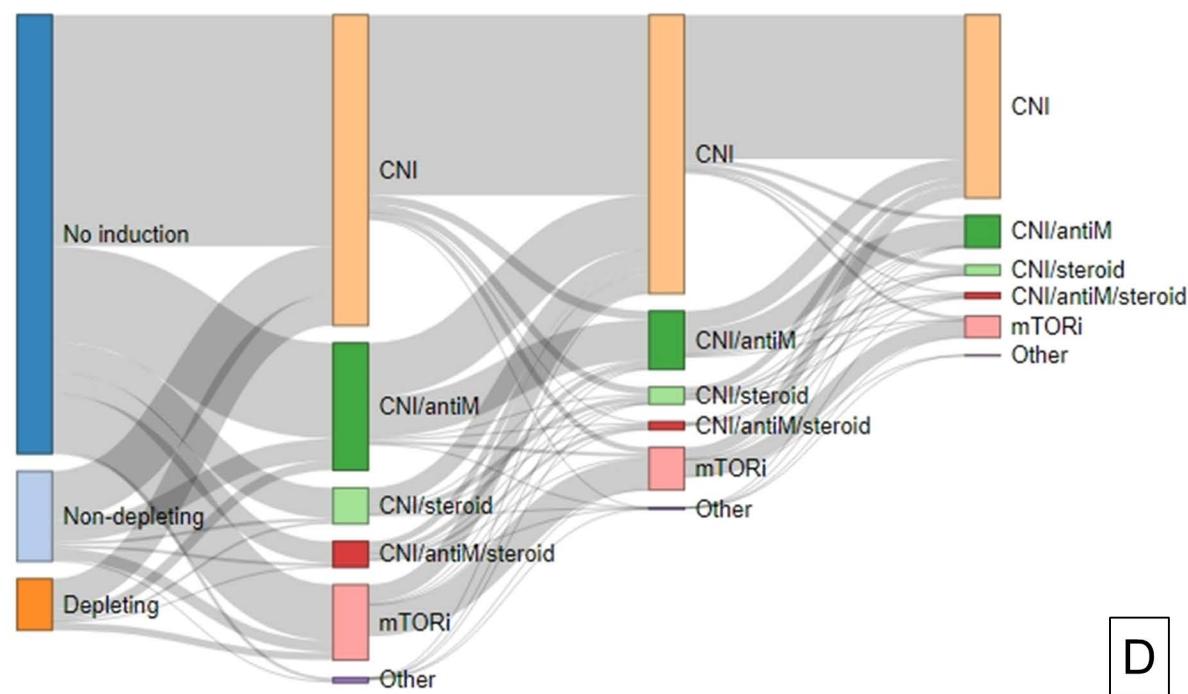
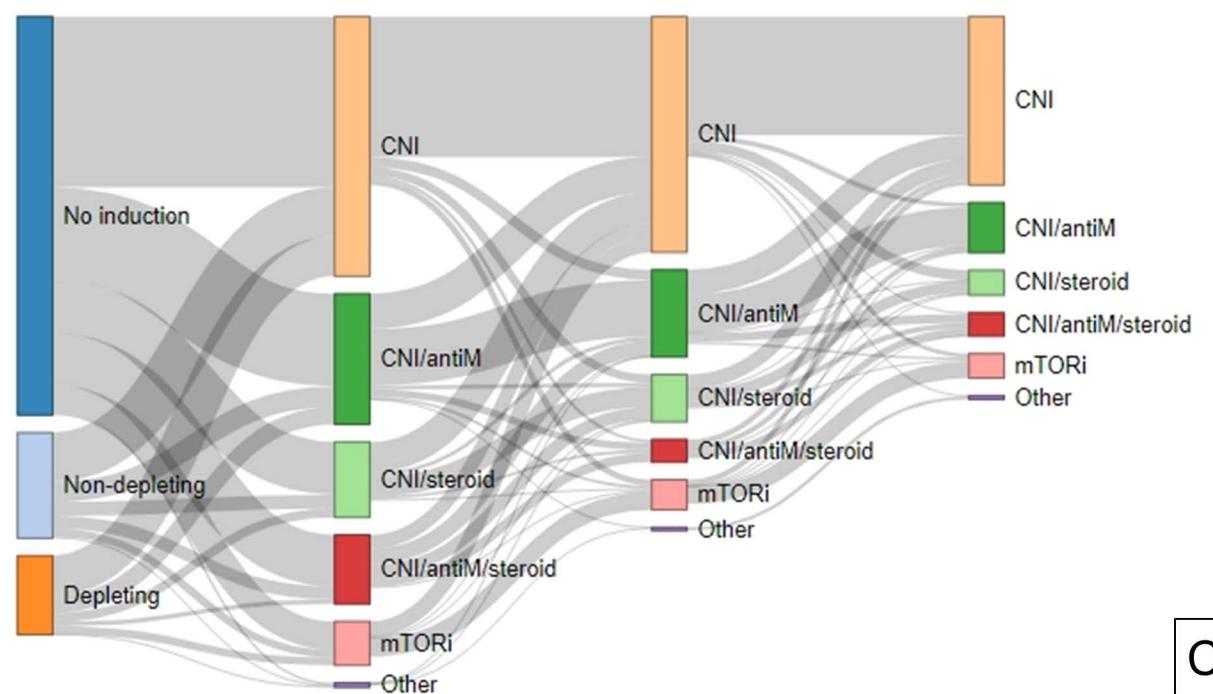
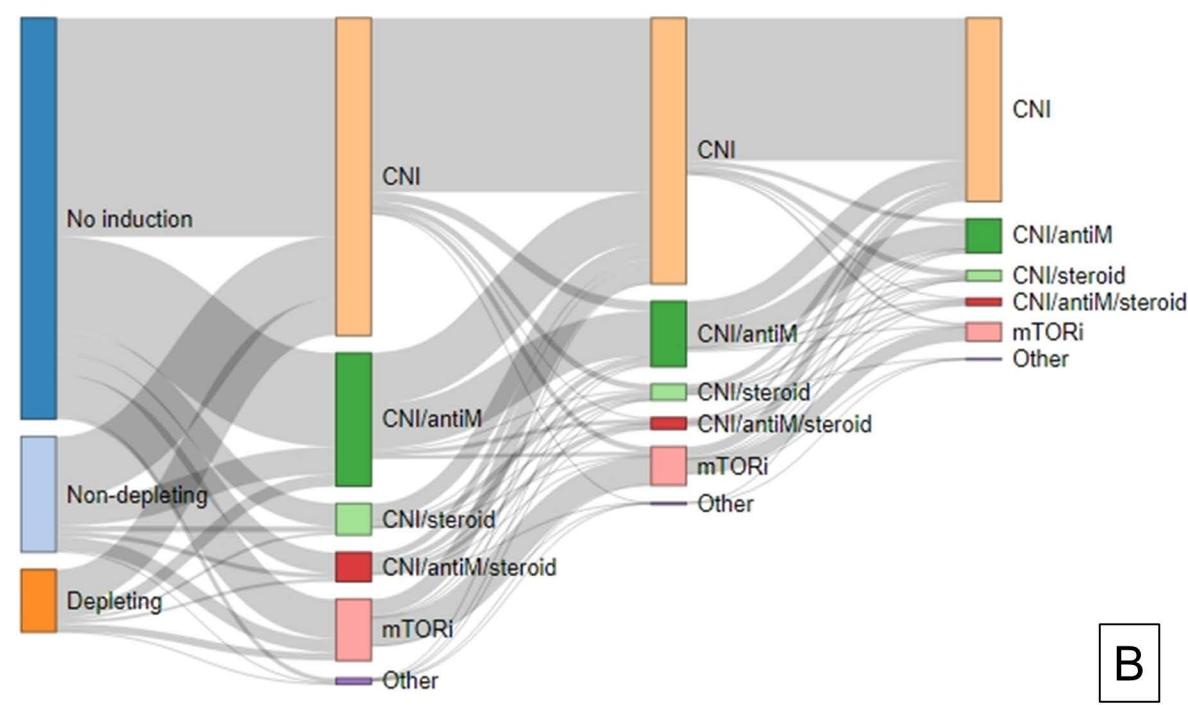
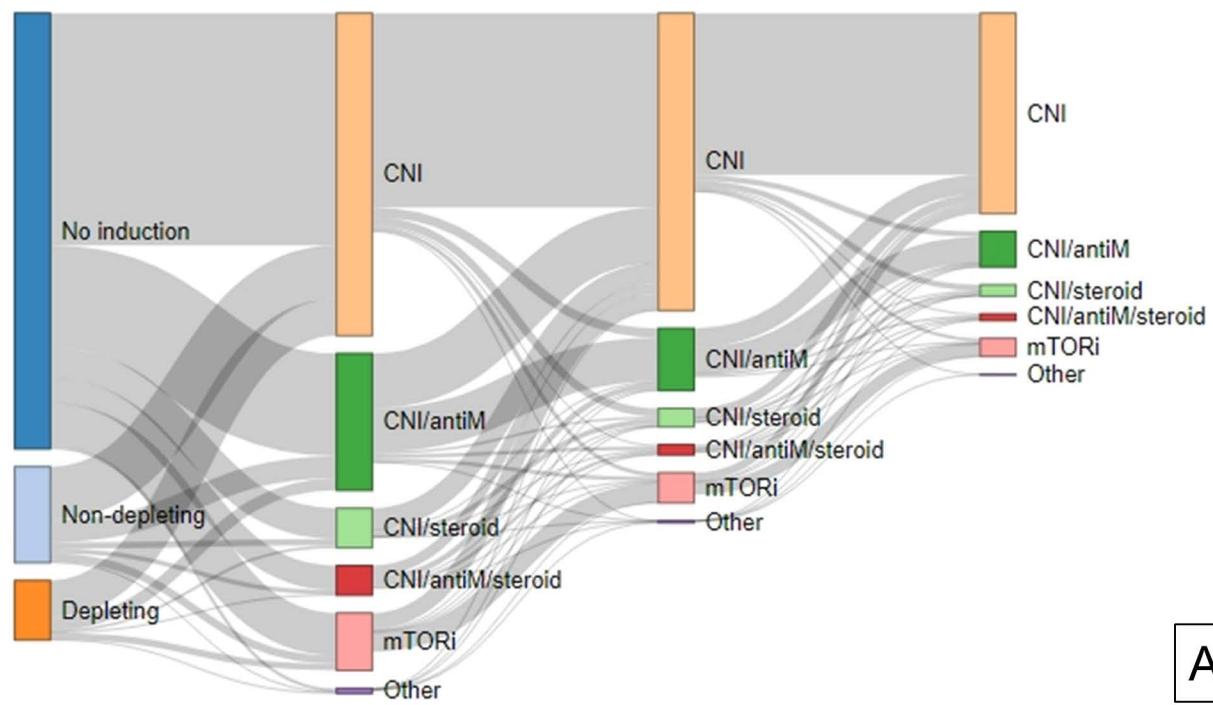
11,639 recipients

Excluded N=313 (2.7%)

- Retransplanted and/or died within 90-days of LT

11,326 recipients in final
UNOS-Medicare study cohort





p<0.001

p<0.001

p=0.074

