Immunosuppressive (IS) treatment patterns following kidney transplant in France: a real-world retrospective cohort using the French national health data system (SNDS) claims database. OISTER Study.

RWD55

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Introduction

- Patients undergoing kidney transplantation require lifelong immunosuppressant (IS) therapy to prevent graft rejection [1].
- Currently, several pharmacological classes of IS are available and routinely used in this therapeutic context.
- In France, the introduction of belatacept (NULOJIX®) at the end of 2011 has broadened the range of IS available [2].
- In France, there are no recent data on the real-life use of IS in kidney transplant patients.
- The French health insurance database provides a powerful epidemiological research tool to assess drug use and treatment regimens at the nationwide level.

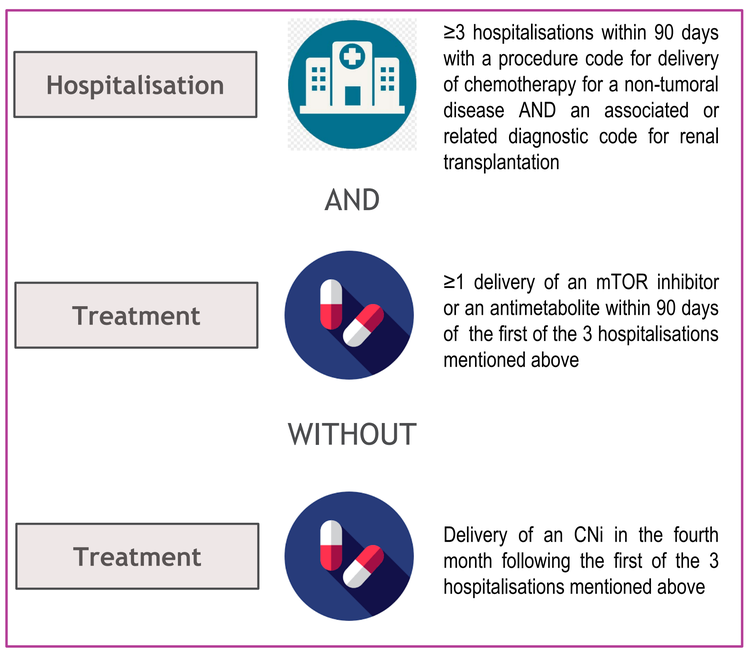
Objective

To describe IS treatments in adult patients undergoing kidney transplantation between 2009 and 2020 using data retrieved from the French national health insurance claims database (SNDS).

Methods

- The OISTER study was a retrospective cohort generated from the SNDS.
- The SNDS contains anonymous information on all reimbursed claims and covers more than 98% of French population [3].
- The cohort comprised all adult patients admitted to hospital between 2009 and 2020 for kidney transplantation (CCAM codes JAE003 or HNEA002).
- Included patients were followed from hospitalisation for kidney transplant (index date) to the first event of interest (death, graft loss, loss to follow up or study end on 31/12/2020).
- IS treatments delivered by community pharmacies were identified from reimbursement data according to Anatomical Therapeutic Chemical codes and packaging identification codes.
- Patients treated with belatacept were identified using an algorithm (Figure 1), then directly in the database when it first became identifiable as a listed drug in the SNDS (April 2020).
- Comorbidities were documented for a historical period going back from the index hospitalisation to early 2008, with a minimum duration of one year.

Figure 1. Identification of patients treated with belatacept



Recruitment

- Between 2009 and 2020, 35,216 patients were hospitalised for a kidney transplant, of whom 34,600 were eligible (Figure 2).
- The number of transplants per year have risen gradually since 2009, until curtailed in 2020 by the COVID epidemic (Figure 3).

References

1. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2022. ISBN 978-94-92671-16-5.
2. Su VC et al. Ann Pharmacother. 2012; 46(1): 57-67. doi: 10.1345/aph.1Q537.
3. Bezin J, et al. *Pharmacoepidemiol Drug Saf*. 2017; 26(8): 954-962. doi: 10.1002/pds.4233.

Acknowledgments

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Figure 2. Patient flow

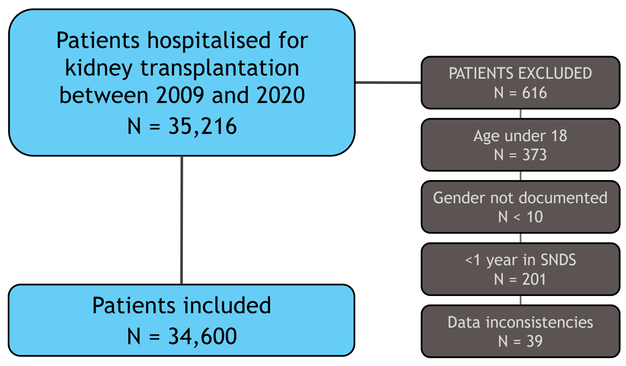
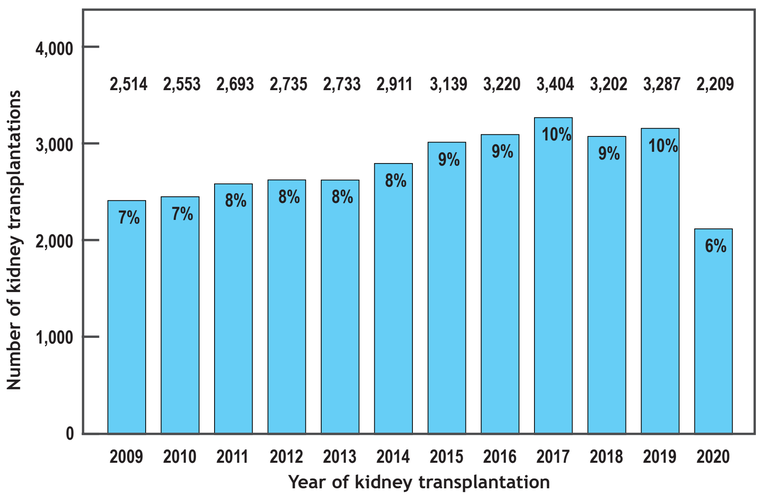


Figure 3. Distribution of study population according to the year of kidney transplantation (N = 34,600)



Patient characteristics

- The majority of patients undergoing kidney transplantation were men (62.7%) (Figure 4).
- The median age of enrolled patients was 54 years [interquartile range: 43 – 64]
- The age distribution of enrolled patients is represented in Figure 5.
- Cardiovascular comorbidities were frequent: 91.9% of patients had hypertension and 45.7% dyslipidaemia (Table 1).

Figure 4. Gender distribution

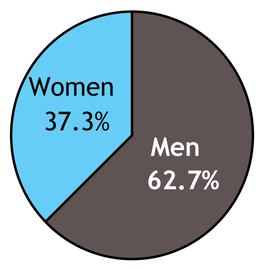


Figure 5. Age distribution

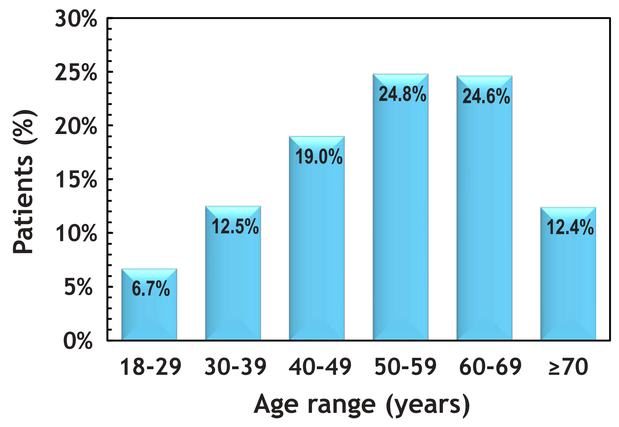


Table 1. Comorbidities

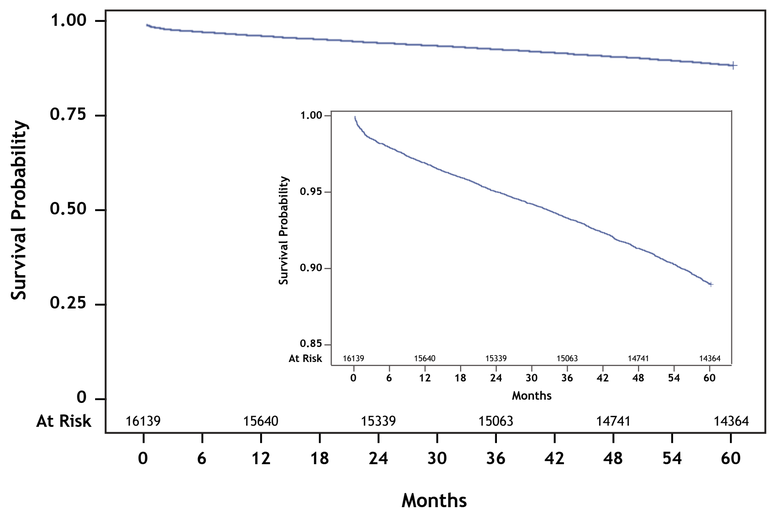
Comorbidities, n (%)	
Hypertension	31,805 (91.9%)
Dyslipidaemia	15,818 (45.7%)
Diabetes	6,806 (19.7%)
Ischaemic heart disease	5,556 (16.1%)
Morbid obesity	4,005 (11.6%)
Heart failure	3,061 (8.8%)
Peripheral artery disease	2,438 (7.0%)
Malnutrition	2,351 (6.8%)
Angina pectoris	927 (2.7%)
History of stroke	659 (1.9%)
History of coronary stent placement	362 (1.0%)

Results

Follow-up

- The median follow-up duration was 4.0 years (IQR: 1.6 – 7.0] .
- The overall survival probability at five years was 0.89 [95%CI: 0.88 - 0.89].
- The Kaplan Meier survival curve is displayed in Figure 5.

Figure 5. Overall survival over 5 years following kidney transplantation (including a zoom of the curve).



Immunosuppressant treatment

- Over the follow-up period, >95% of patients received a calcineurin inhibitor, a corticosteroid and an antimetabolite at least once (Table 2).

Table 2. Immunosuppressant treatment over the follow-up period

Treatment	Year of kidney transplantation			
	2009 - 2019 (N = 32,391)	2009 - 2011 (N = 7,760)	2012 - 2015 (N = 11,518)	2016 - 2019 (N = 13,113)
At least one IS	29,933 (92.4%)	7,161 (92.3%)	10,701 (92.9%)	12,071 (92.1%)
Calcineurin inhibitor (CNi)	29,573 (98.8%)	7,082 (98.9%)	10,564 (98.7%)	11,927 (98.8%)
Tacrolimus	*26,051 (88.1%)*	*5,874 (99.0%)*	*9,239 (87.5%)*	*10,938 (91.7%)*
Ciclosporine	*6,518 (22.0%)*	*2,110 (29.8%)*	*2,587 (24.5%)*	*1,821 (15.3%)*
Corticosteroids (CS)	28,536 (95.3%)	6,898 (96.3%)	10,245 (95.7%)	11,393 (94.4%)
Antimetabolites	29,318 (97.9%)	7,098 (99.1%)	10,509 (98.2%)	11,711 (97.0%)
Mycophenolic acid	*28,900 (98.6%)*	*7,029 (99.0%)*	*10,341 (98.4%)*	*11,530 (98.5%)*
mTOR inhibitors	5,231 (17.5%)	1,560 (21.8%)	1,859 (17.4%)	1,812 (15.0%)
Belatacept	1,272 (4.2%)	172 (2.4%)	587 (5.5%)	513 (4.2%)
Combination therapy of drug classes in patients treated by an IS, (belatacept excluded):	N = 29,933	N = 7,161	N = 10,701	N = 12,071
CNi + antimetabolite	28,837 (96.3%)	7,001 (97.8%)	10,338 (96.6%)	11,498 (95.3%)
CNi + mTOR inhibitor	3,598 (12.0%)	678 (9.5%)	1,332 (12.4%)	1,598 (13.2%)
mTOR inhibitor + antimetabolite	1,789 (6.0%)	1,004 (14.0%)	586 (5.5%)	199 (1.6%)
CNi + mTOR inhibitor + antimetabolite	846 (2.8%)	393 (5.5%)	287 (2.7%)	166 (1.4%)
Combination therapy of drug classes in patients treated by belatacept:	N = 1,272	N = 172	N = 587	N = 513
Belatacept + antimetabolite + CS	985 (77.4%)	125 (72.7%)	462 (78.7%)	398 (77.6%)

The same therapeutic classes were used as initial treatment in the three months following the transplant (Table 3).
Belatacept was identified in 4.2% of patients overall and in 1.0% of patients in the three months following transplantation.
Treatment patterns have been relatively stable over time.

Table 3. Immunosuppressant treatment during the three months following transplantation

Treatment	Year of kidney transplantation			
	2009 - 2019 (N = 32,391)	2009 - 2011 (N = 7,760)	2012 - 2015 (N = 11,518)	2016 - 2019 (N = 13,113)
At least one IS	29,453 (90.9%)	6,948 (89.5%)	10,536 (91.5%)	11,969 (91.3%)
Calcineurin inhibitor (CNi)	28,270 (96.0%)	6,438 (92.7%)	10,096 (95.8%)	11,736 (98.1%)
Tacrolimus	*23,925 (84.6%)*	*4,946 (76.8%)*	*8,399 (83.2%)*	*10,580 (90.1%)*
Ciclosporine	*4,849 (17.2%)*	*1,590 (24.7%)*	*1,899 (18.8%)*	*1,360 (11.6%)*
Corticosteroids (CS)	26,712 (90.7%)	6,323 (91.0%)	9,481 (90.0%)	10,908 (91.1%)
Antimetabolites	27,942 (94.9%)	6,529 (94.0%)	10,010 (95.0%)	11,403 (95.3%)
Mycophenolic acid	*27,475 (98.3%)*	*6,445 (98.7%)*	*9,810 (98.0%)*	*11,220 (98.4%)*
mTOR inhibitor	1,549 (5.3%)	284 (4.1%)	445 (4.2%)	820 (6.9%)
Belatacept	288 (1.0%)	<10 (-%)	125 (1.2%)	161 (1.3%)
Combination therapy of drug classes in patients treated by an IS, (belatacept excluded):	N = 29,453	N = 6,948	N = 10,536	N = 11,969
CNi + antimetabolite	27,127 (92.1%)	6,315 (90.9%)	9,720 (92.3%)	11,092 (92.7%)
CNi + mTOR inhibitor	1,083 (3.7%)	53 (0.8%)	306 (2.9%)	724 (6.0%)
mTOR inhibitor + antimetabolite	268 (0.9%)	158 (2.3%)	90 (0.9%)	20 (0.2%)
CNi + mTOR inhibitor + antimetabolite	144 (0.5%)	65 (0.9%)	31 (0.3%)	48 (0.4%)
Combination therapy of drug classes in patients treated by belatacept:	N = 288	N = <10	N = 125	N = 161
Belatacept + antimetabolite + CS	188 (65.3%)	<10 (-%)	85 (68.0%)	102 (63.4%)

Conclusions

- The number of kidney transplantations performed each year has been rising over the last decade, with more than 3,200 transplantations each year between 2016 and 2019.
- Survival five years after kidney transplantation is good (89%), considering the patients' characteristics.
- A large majority of patients (>84%) initiated an IS regimen during the maintenance phase which adhered to current practice guidelines [1].
- Treatment patterns have remained stable over the last 12 years.
- It will be interesting to follow trends in IS use over the coming years, as belatacept becomes more widely available.

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