

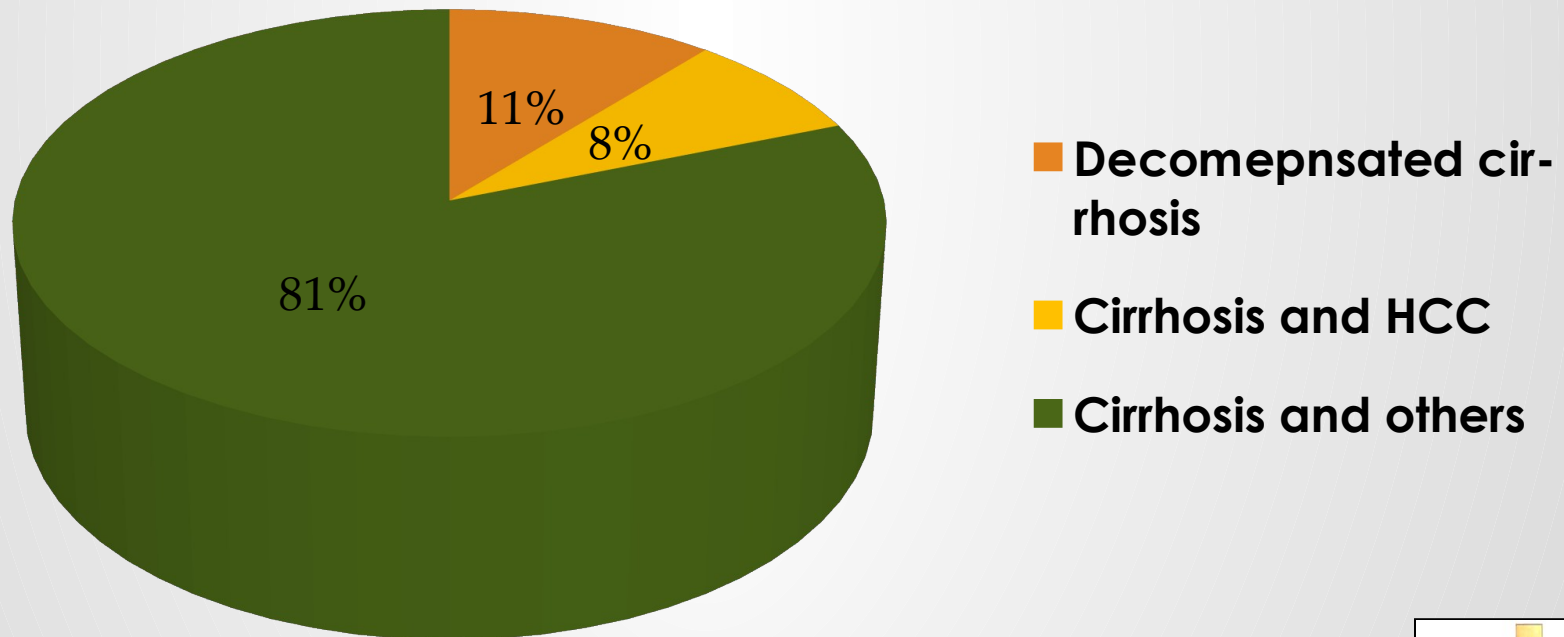
Treatment of HCV cirrhosis and transplanted patients: when and how ?

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HCV: indications for transplantation

- ✓ 2006-2015 : 1061 transplantations in Beaujon
- ✓ 205 (19%) transplantation for HCV cirrhosis ± HCC



HCV and transplantation: natural history

- **Candidate for transplant**

- Treatment failure
- HCV-RNA positive

- **Recurrence after LT**

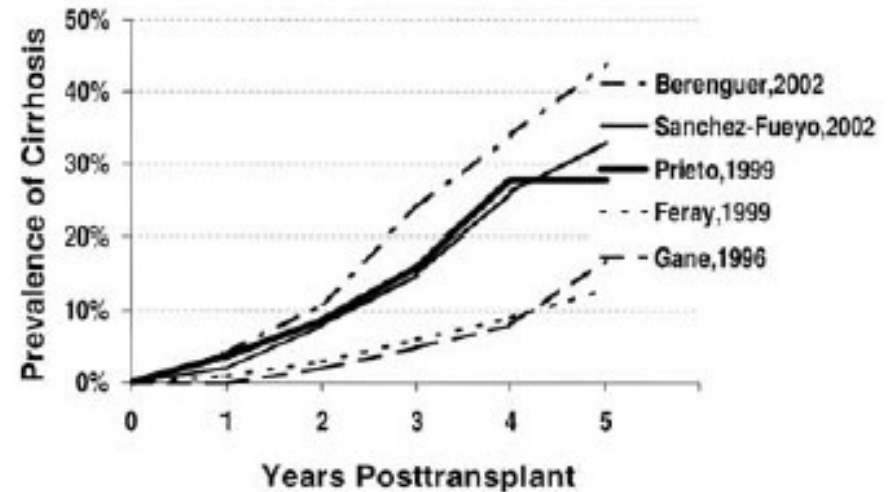
- **Viral replication ↗**

- Immunosuppression

- **Liver fibrosis ↗**

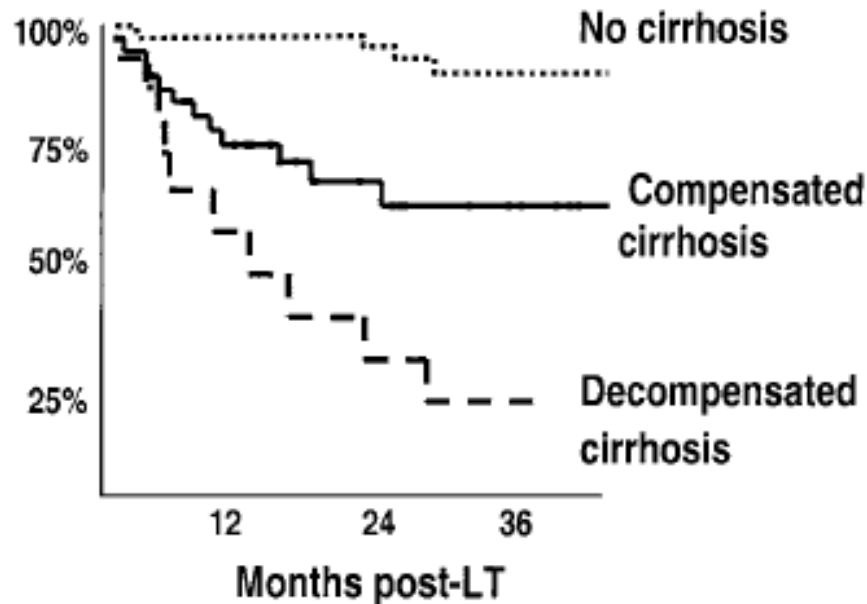
- **Impact on survival**

- Graft loss



Post-transplant recurrence

- **Risk factors:**
 - « Elder » donor
 - Risk ↗ over 40 y
 - Steroid boluses for rejection
 - Induction IS
 - Anti-thymocyte globulins
 - Ciclo vs tacro ?



Treat HCV before transplantation to prevent post transplant recurrence

First generation protease inhibitors and cirrhosis

	Telaprevir	Boceprevir
Patients	299	212
Child A	95%	93%
Genotype 1	89%	90%
Sustained virological response	52%	43%
Serious adverse event	53%	44%
Prematurely discontinuation	48%	46%

Death: 2.2%

Risk factors: Albumin < 35g/L

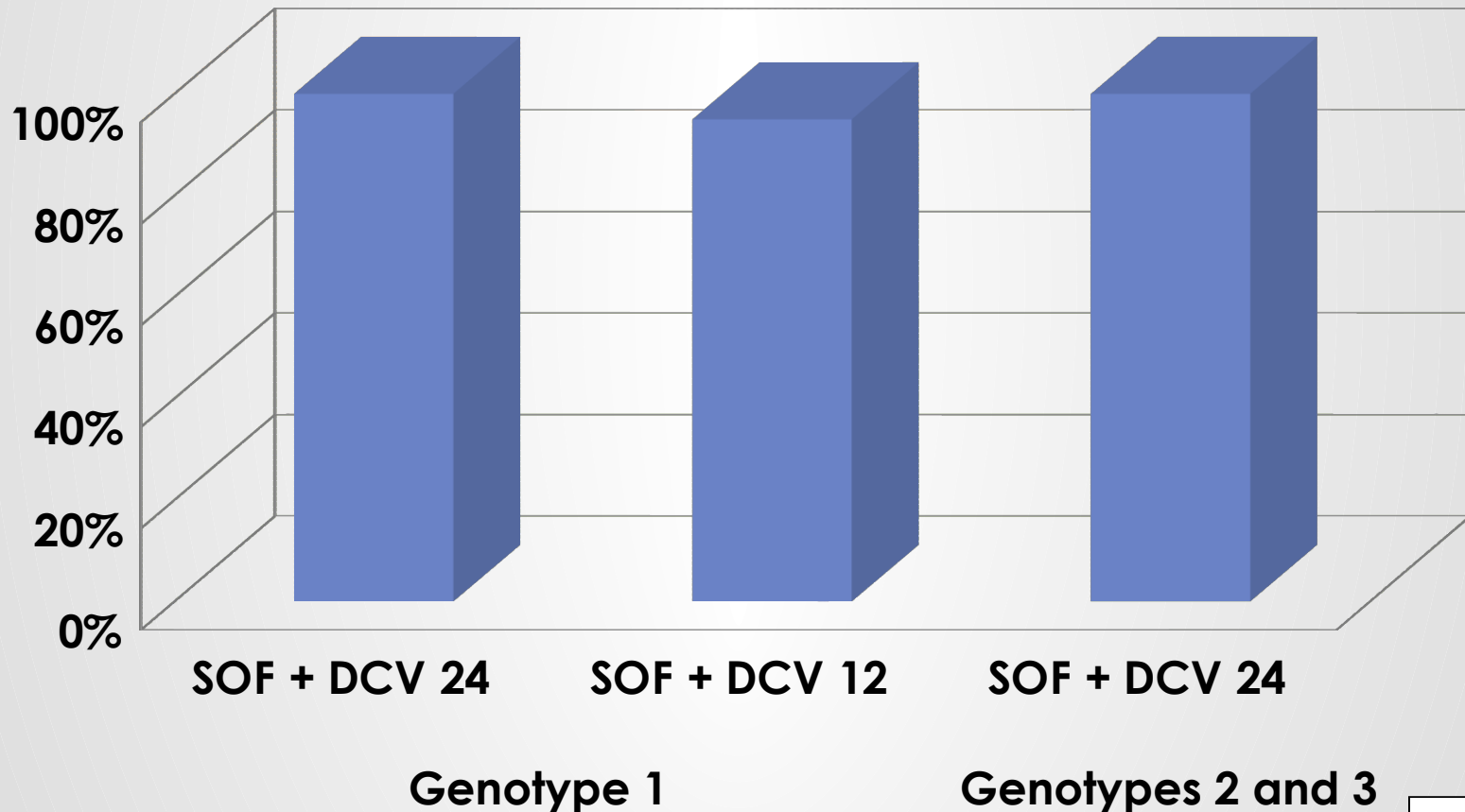
Platelets < 100*10⁹/L

- Hézode C et al. Gastroenterology 2014; 147: 132



Direct antiviral agents

Naive and previously treated HCV-infected patients



- Sulkowski MS et al. N Engl J Med 2014; 370: 211.



Antiviral therapy and cirrhosis: safety

	Peg IFN + Boce + Riba	Sofo + riba
Author	Hézode C	Curry MP
Year	2014	2015
Serious adverse event	32	18
Anemia (<9g/dL, %)	23	5
Transfusion (%)	6	0
Decompensation (%)	3	0
Early discontinuation (%)	26	3

Hézode C et al. Gastroenterology 2014; 147: 132
Curry MP et al. Gastroenterology 2015; 148: 100



Antiviral agents and transplantation: issues to be addressed

- **Before transplantation**

- Reverse the complications of cirrhosis
 - Removed from the waiting list
- Prevent post transplant recurrence
 - Undetectable HCV-RNA at the time of transplantation

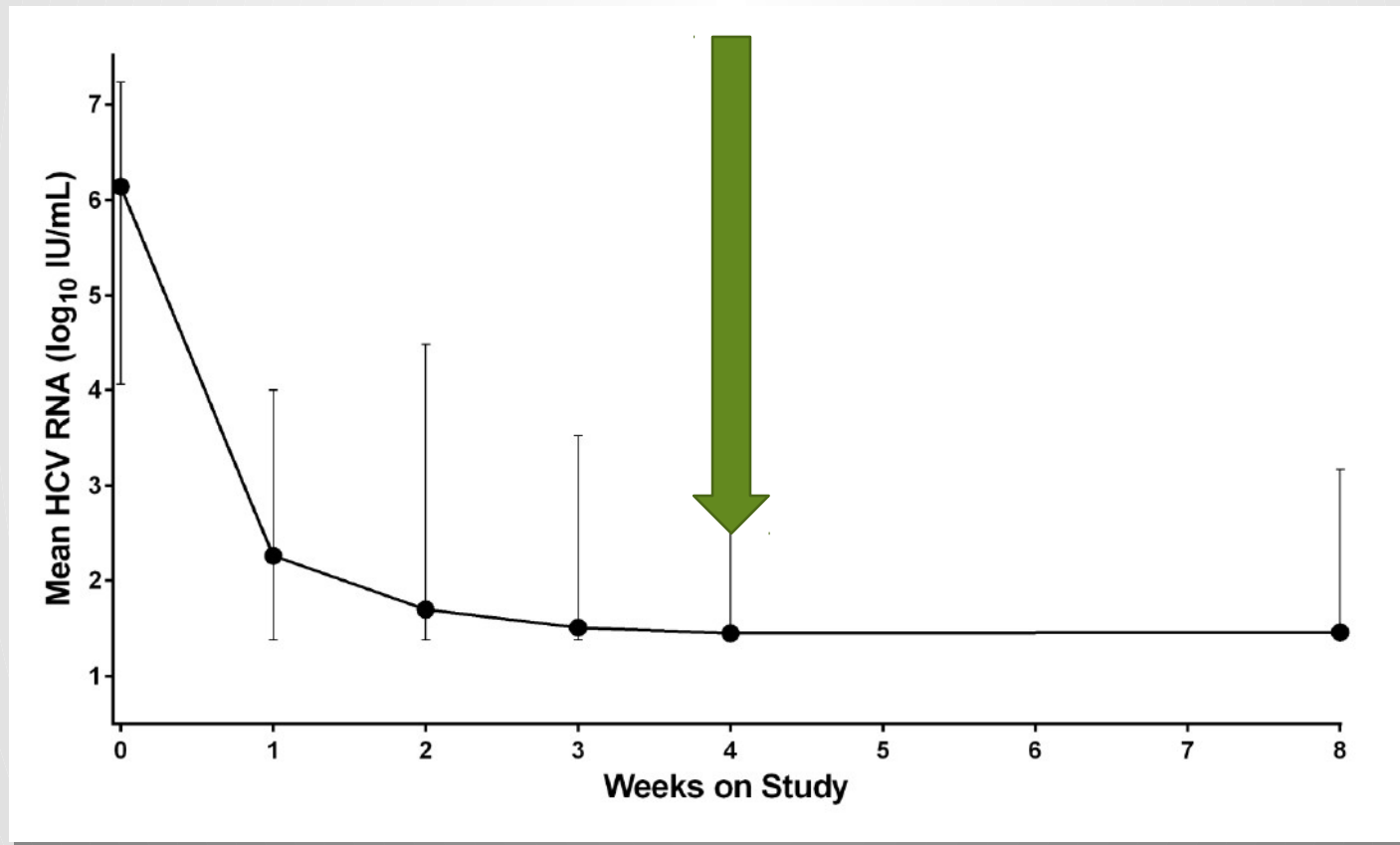
- **After transplantation**

- Treat HCV recurrence
- Prevent graft failure/retransplantation



Sofosbuvir + ribavirin

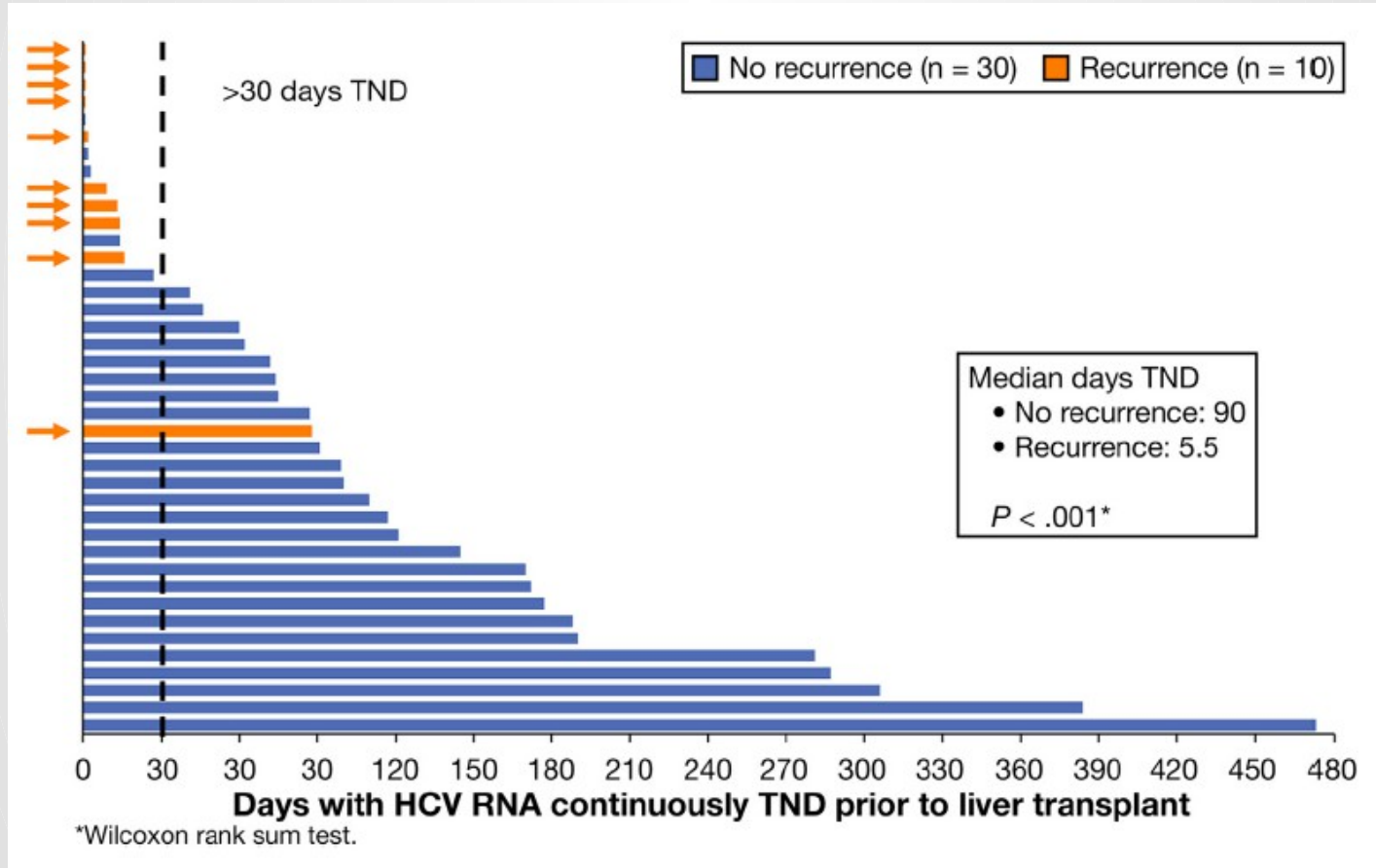
Achieve HCV-RNA negative status



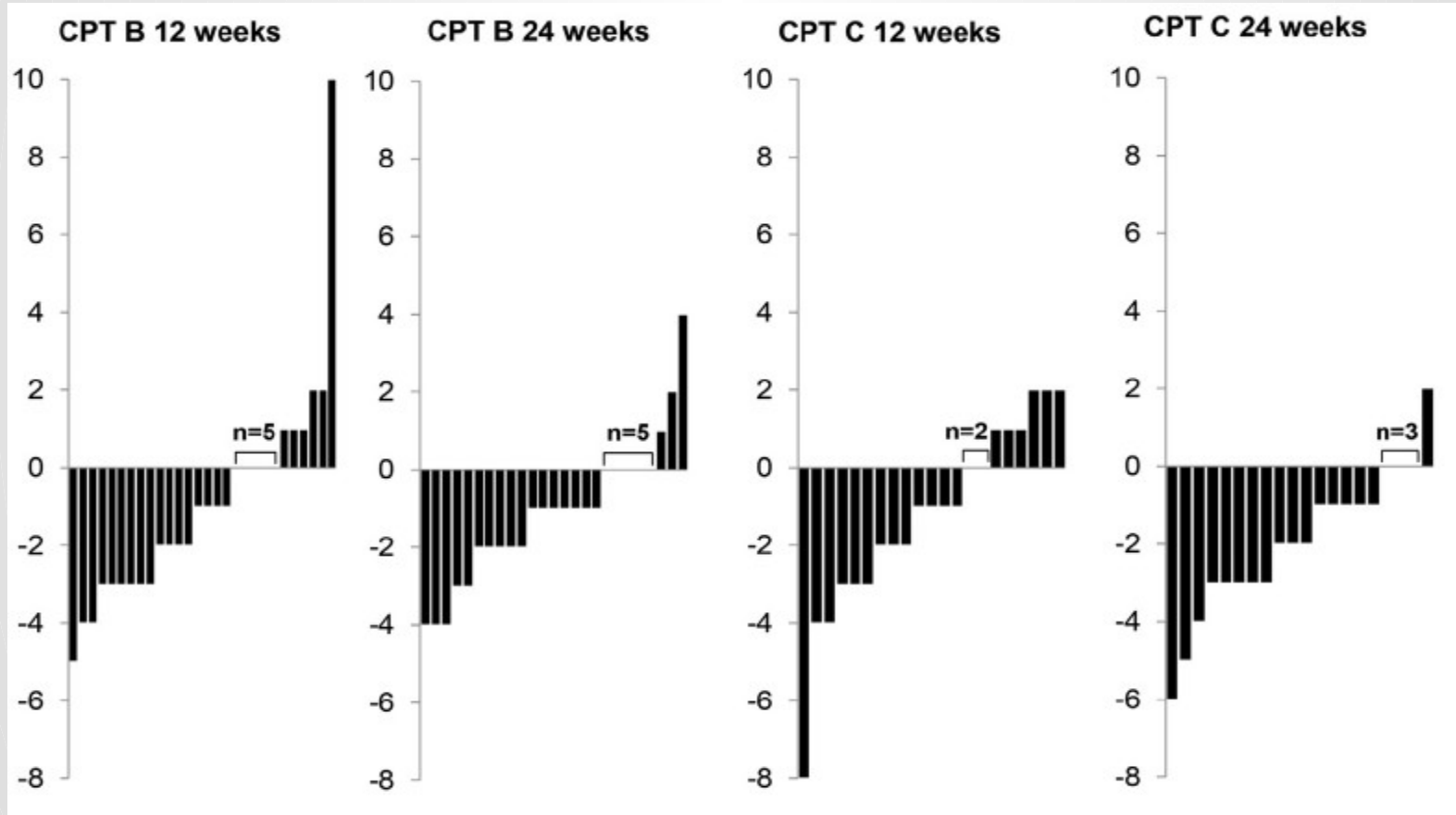
Curry MP et al. Gastroenterology 2015; 148: 100



Sofosbuvir + ribavirin to prevent post-transplant recurrence



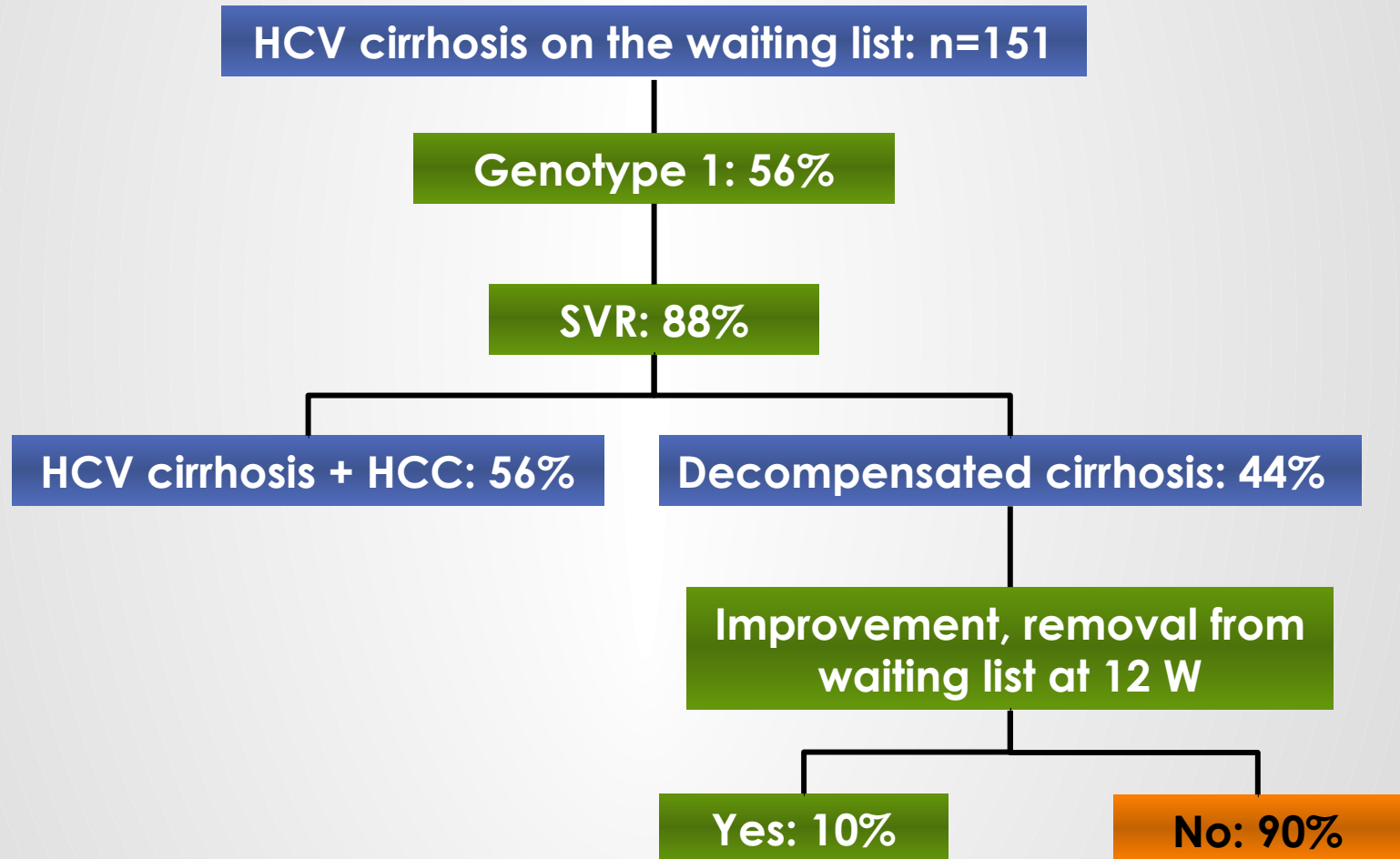
Impact of SVR on disease severity: MELD score



- Charlton M Gastroenterology 2015; 149: 649.

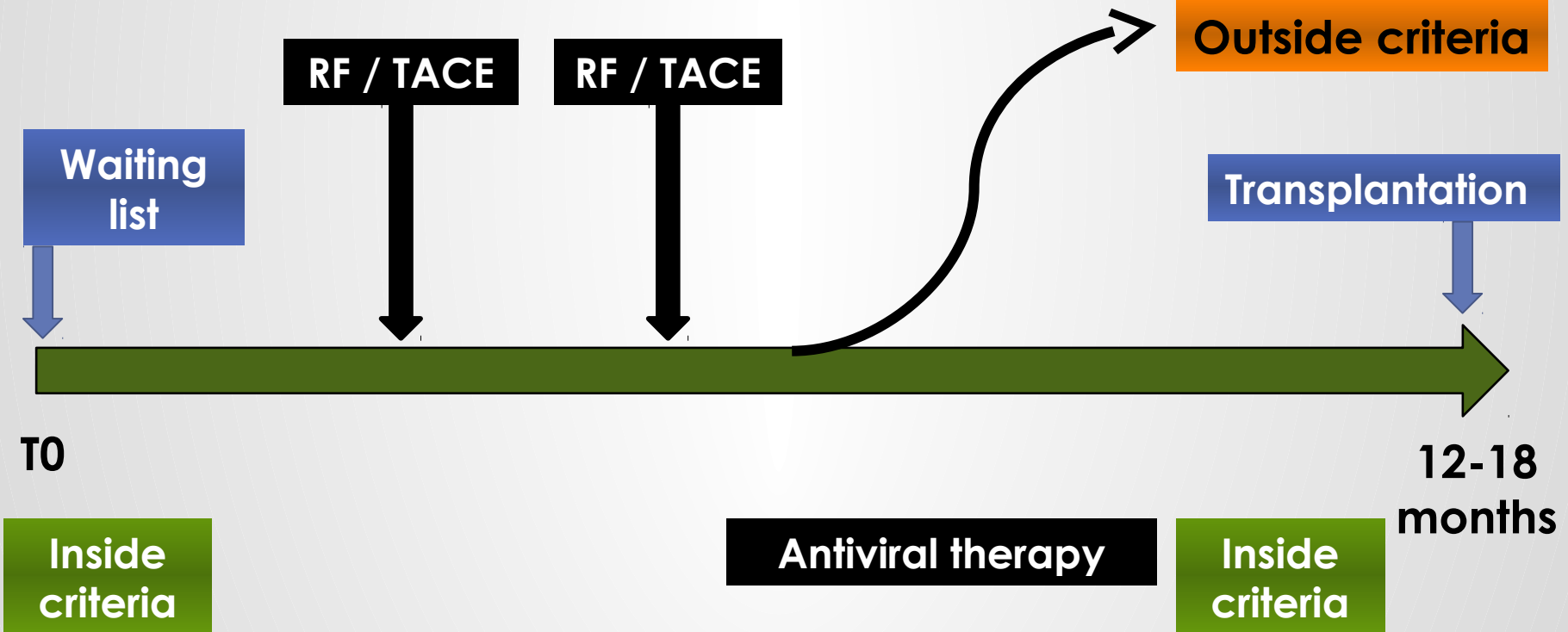


Sofosbuvir-based therapy impact on the outcome

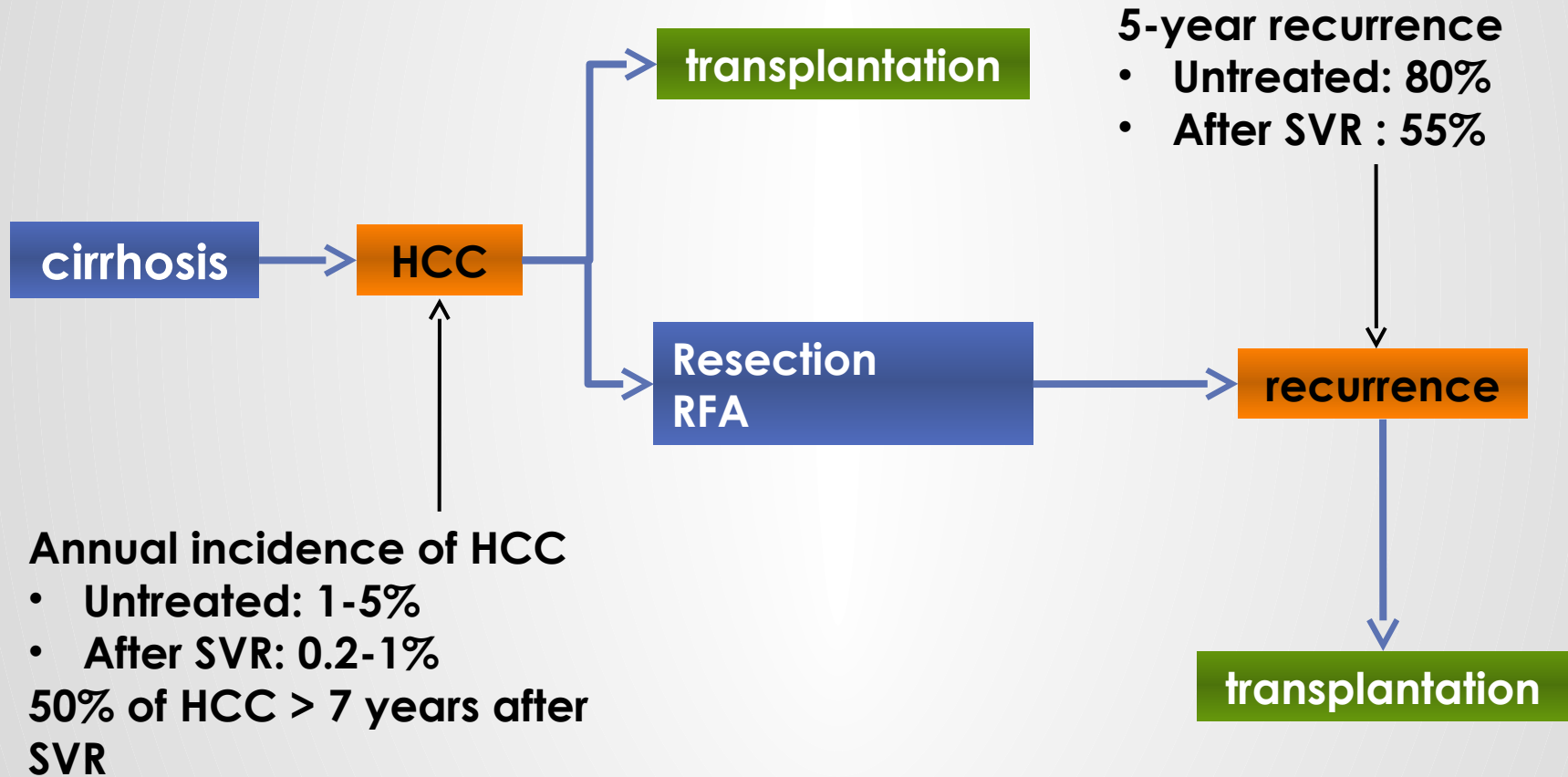


HCV cirrhosis and HCC

HCV cirrhosis + HCC on the waiting list : 66% Child A

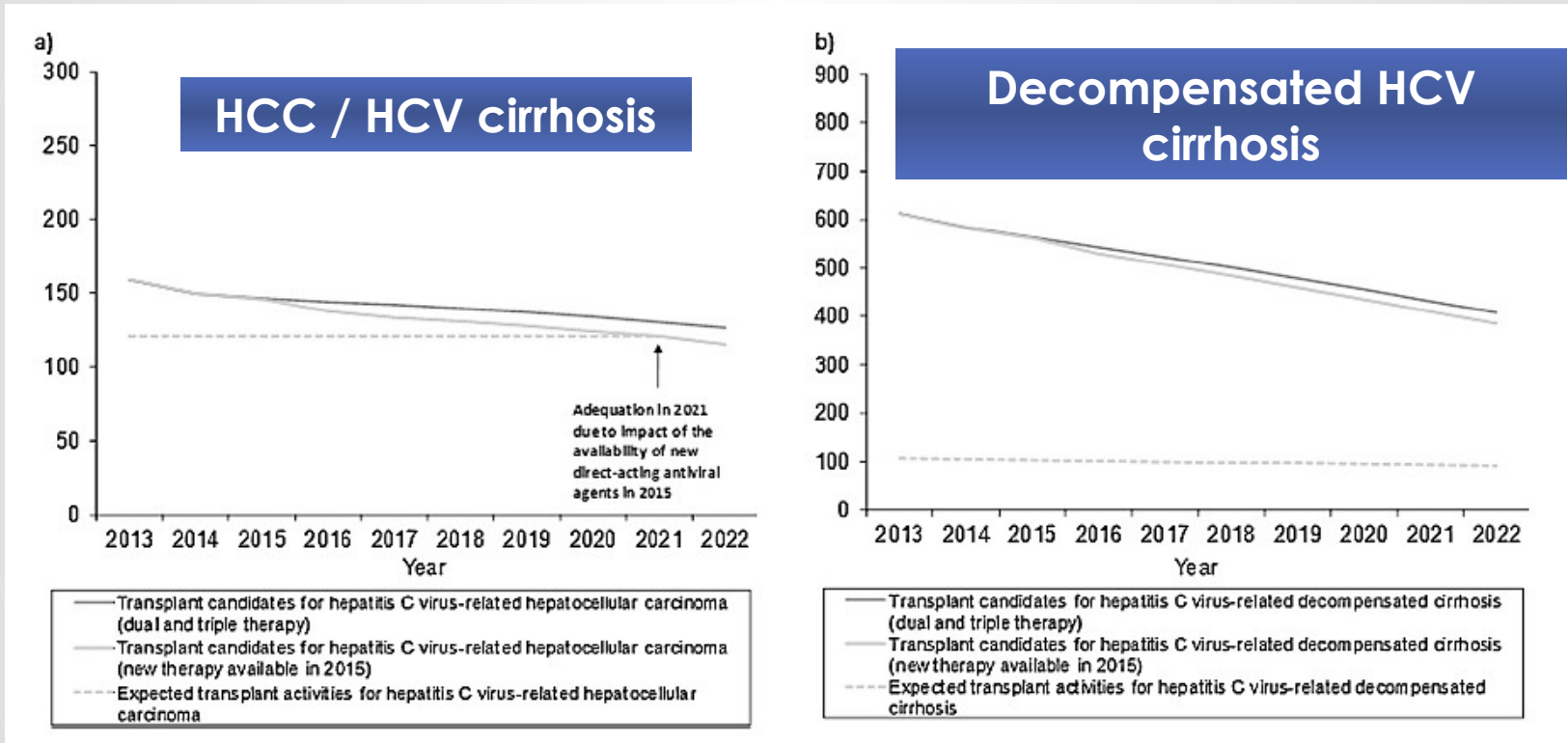


Antiviral agents: impact on HCC



Van de Meer AJ et al. JAMA 2012; 308: 2584.
Zhang W et al. Mol Clin Oncol 2014; 2: 1125.

Antiviral therapy and the need for transplantation

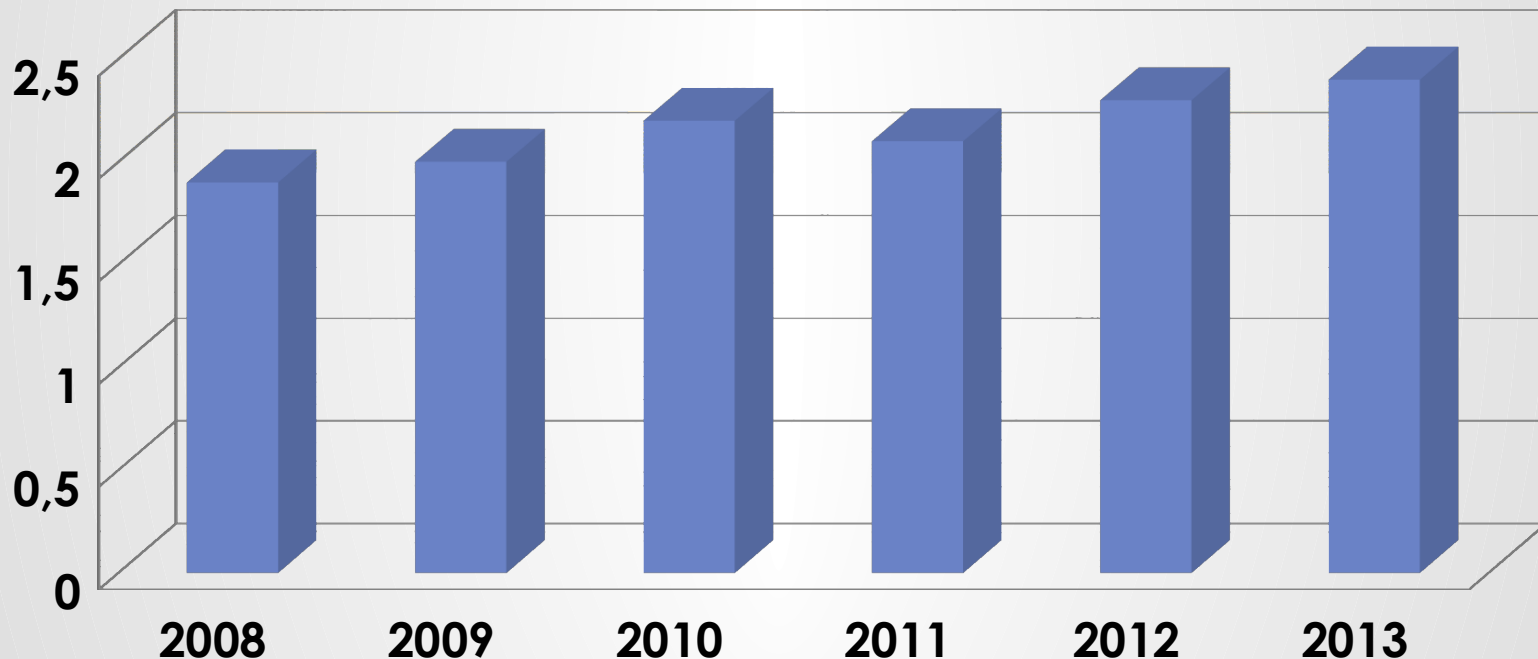


Deuffic-Burban S et al. Dig Dis Sci 2014; 46: 157.



Imbalance between donors and recipients

Candidates / donors in France



• Data: Agence de la Biomédecine



Take home messages

- **When to start antiviral therapy pre-transplant?**
 - Compensated HCV cirrhosis and HCC: 2-3 months before transplant
 - Decompensated cirrhosis: at listing
- **Which treatment ?**
 - Compensated HCV cirrhosis and HCC, non-3 genotype
 - (Sofo + lédi + riba) or (sofo + dacla + riba)
 - Ombitasvir + paritaprevir + ritonavir ?
 - Compensated HCV cirrhosis and HCC, genotype 3
 - Sofo + dacla + riba
 - Decompensated cirrhosis
 - (Sofo + lédi)or (sofo + dacla) (G3)



Take home messages

- **How long?**
 - Careful approach = 24 W
 - 12 W possibly enough with riba
- **Pitfalls:**
 - Protease inhibitors in Child B-C cirrhosis
 - Continue therapy post transplant in patients receiving DAAs for more than 2 months pre transplant and HCV-RNA neg
 - Initiate antiviral therapy in candidates with HCC that is not controlled



Take home messages

- **What can be expected?**
 - Prevent post transplant recurrence
 - Improve cirrhosis with a possibility for removal from the waiting list ?
 - Slowing HCC progression ?
- **Reduction in the number of transplantations for HCV-cirrhosis \pm HCC**
- **No reduction in the number of transplantations**

