

CERTICAN NORDIC TRIAL IN RENAL TRANSPLANTATION (the CENTRAL study)

Mjörnstedt L¹, Sørensen SS², von Zur Muhlen B³,
Jespersen B⁴, Melchior J⁵, Bistrup C⁶, Andersson H⁷,
Gustafsson B¹, Undset LH⁸, Solbu D⁹, Holdaas H⁸

1. Sahlgrenska University Hospital, Gothenburg, Sweden
2. Rigshospitalet, Copenhagen University Hospital, Denmark
3. Uppsala University Hospital, Sweden
4. Skejby Hospital, Aarhus, Denmark
5. Herlev Hospital, Denmark
6. Odense University Hospital, Denmark
7. Skåne University Hospital, Malmö, Sweden,
8. Oslo University Hospital, Norway
9. Novartis Pharma Scandinavia

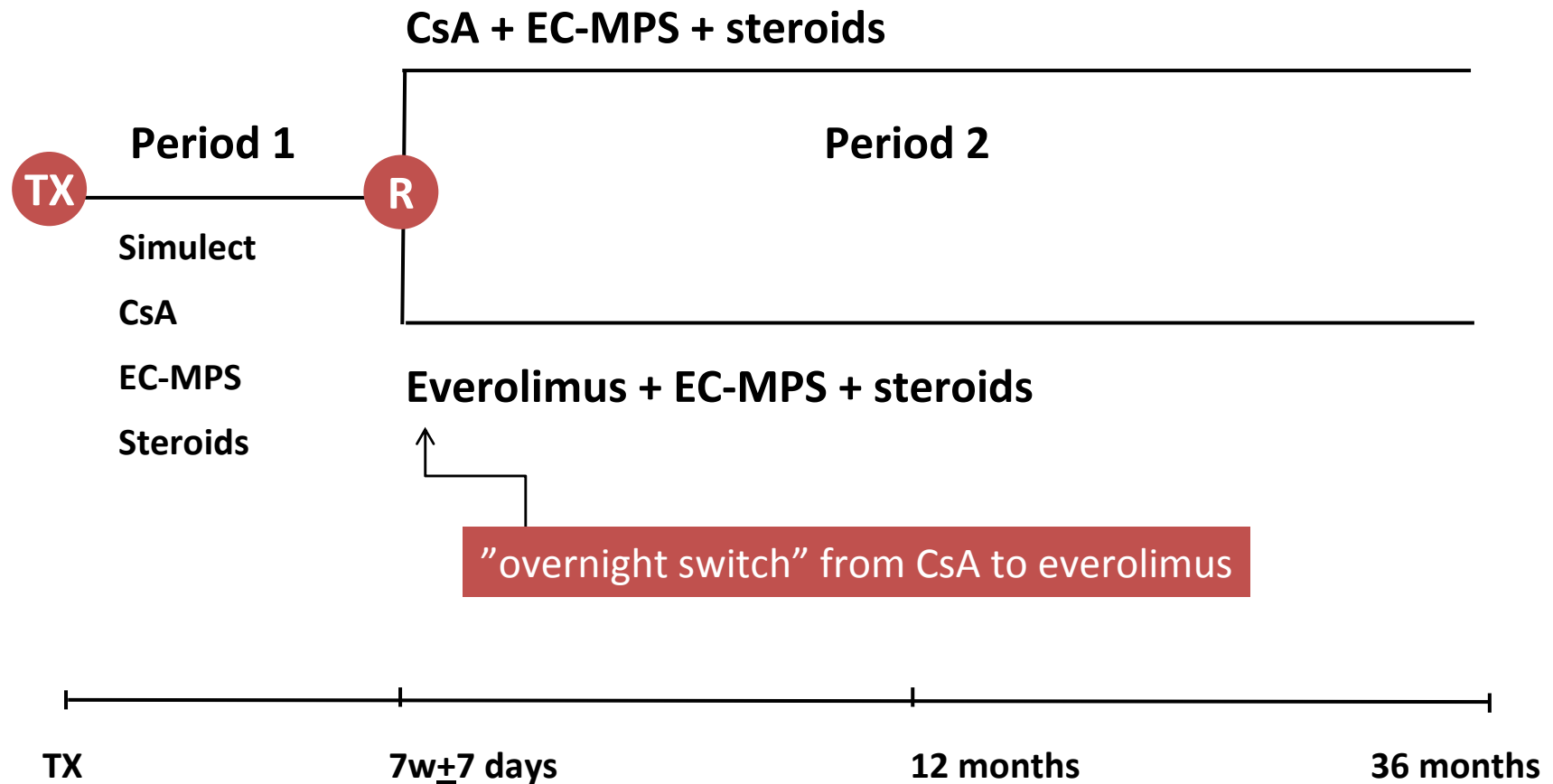
Study purpose

A controlled randomized open-label multicentre study evaluating if early protocol conversion to everolimus from cyclosporine in the novo renal transplant recipients can improve long-term renal function

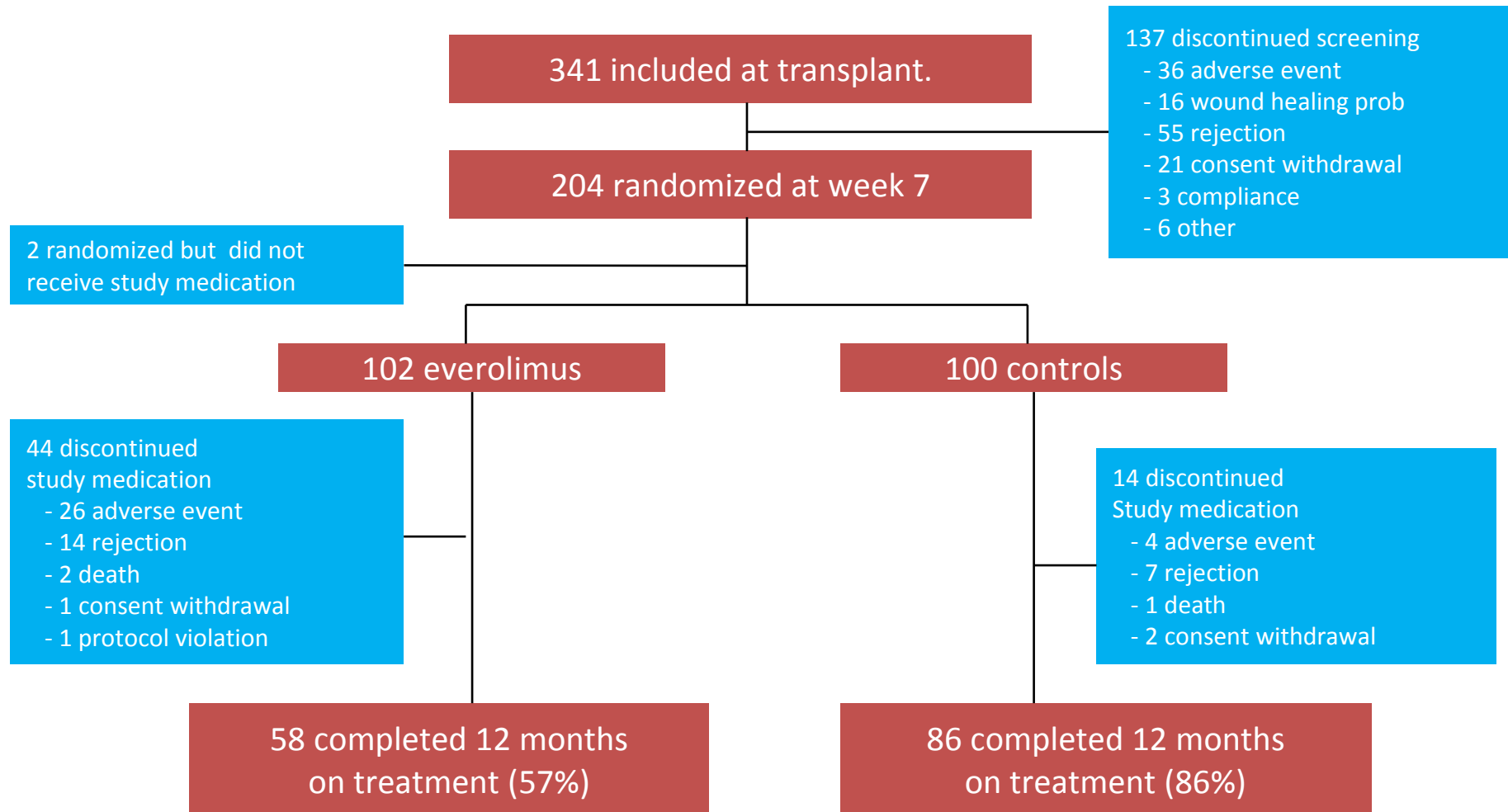
Primary objective

To compare the treatment regimens by assessing the difference in renal function evaluated by measured glomerular filtration rate (mGFR) 12 months after renal transplantation (TX)

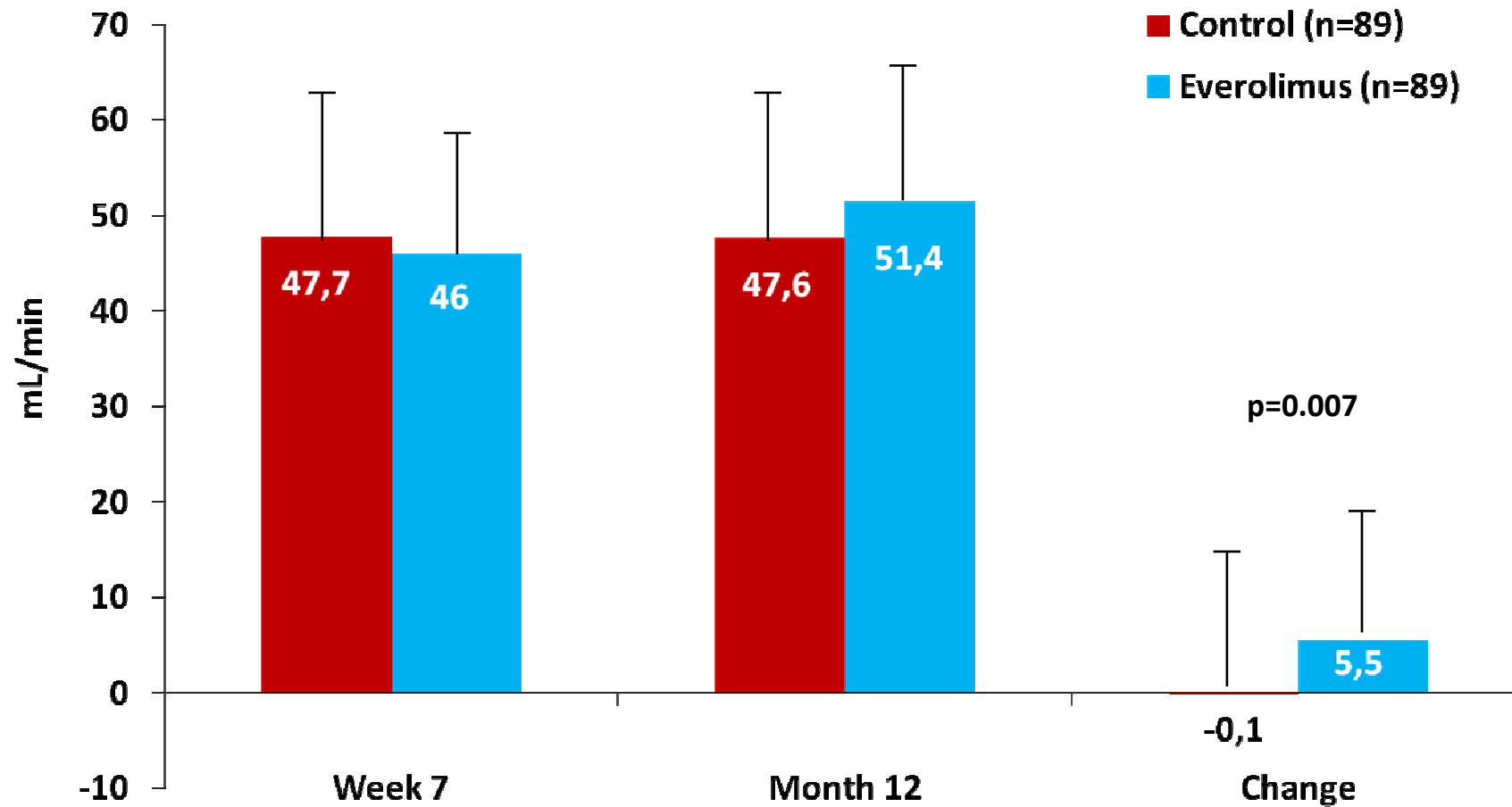
CENTRAL – Design



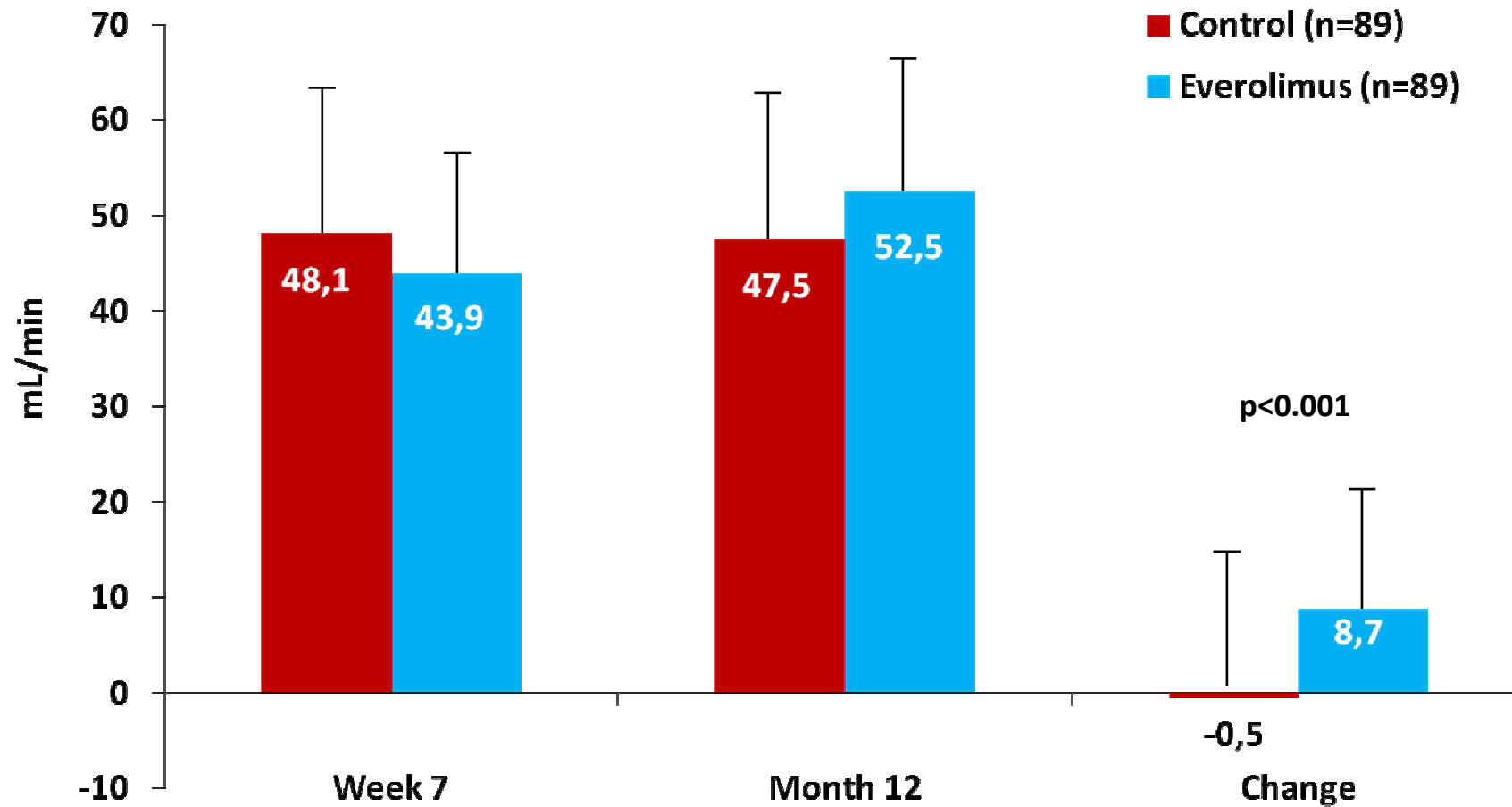
Patient disposition



Primary endpoint: Measured GFR (ITT analysis)

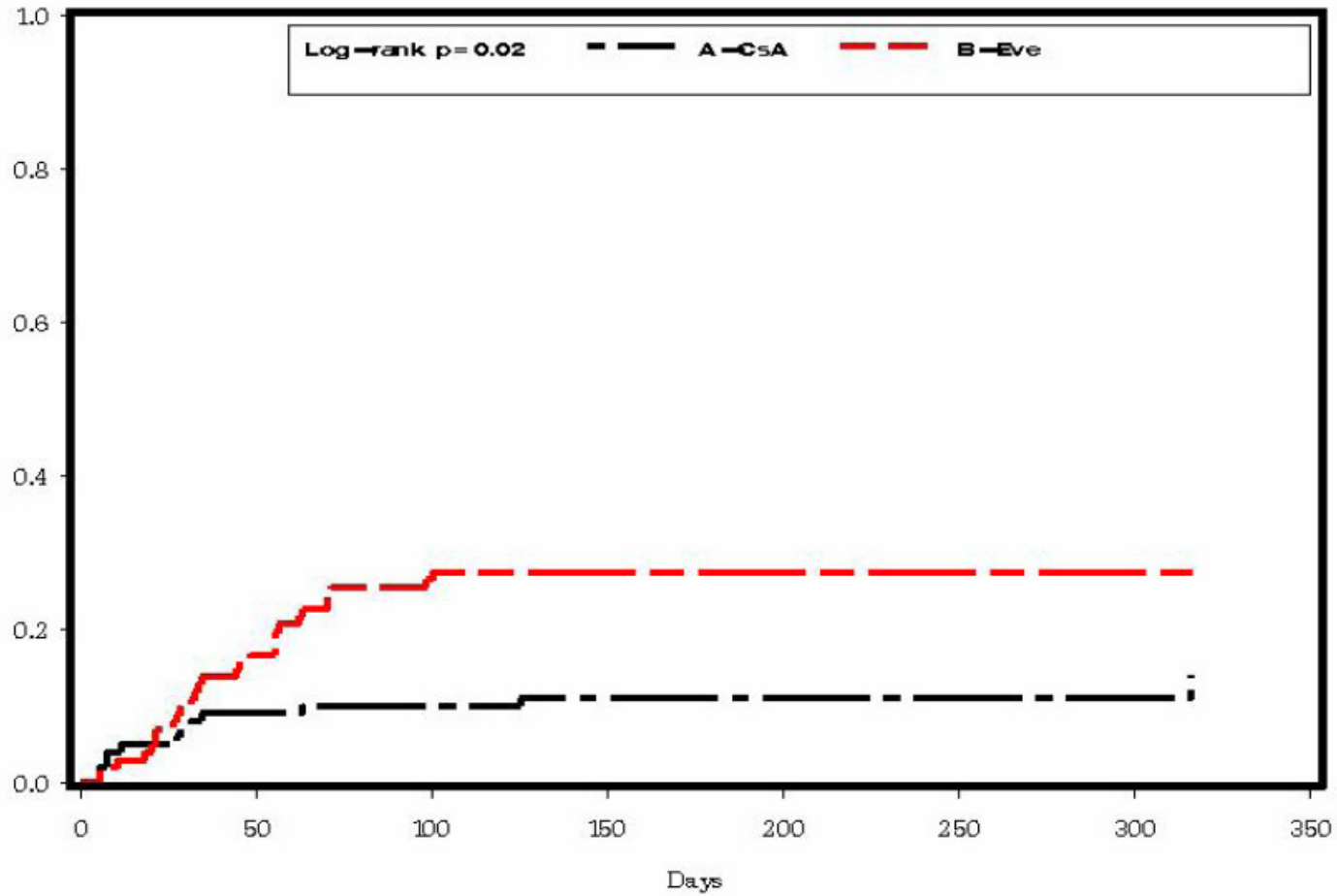


Primary endpoint: Measured GFR (PP analysis)

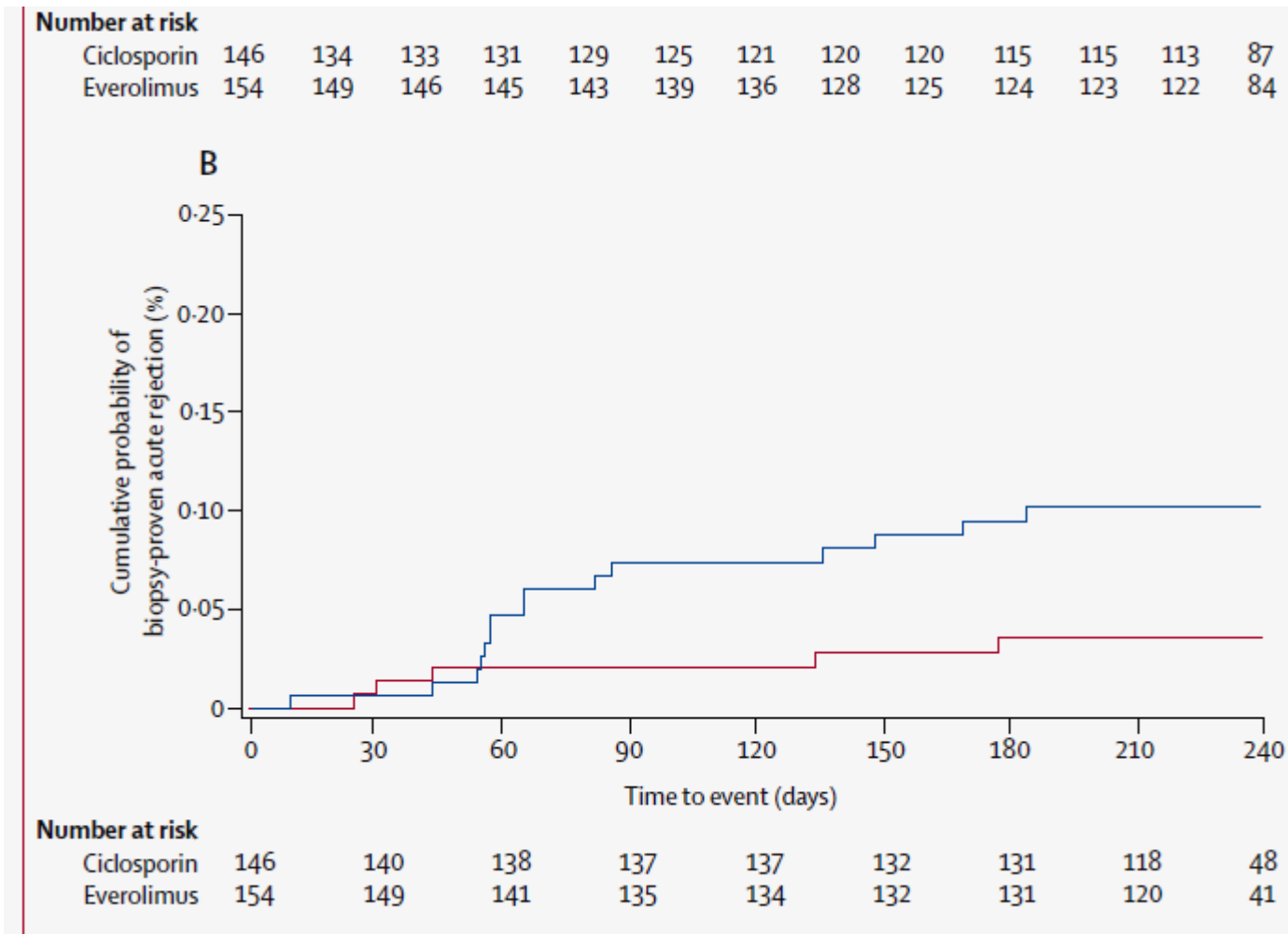


Time to first BPAR

Proportion
of
patients



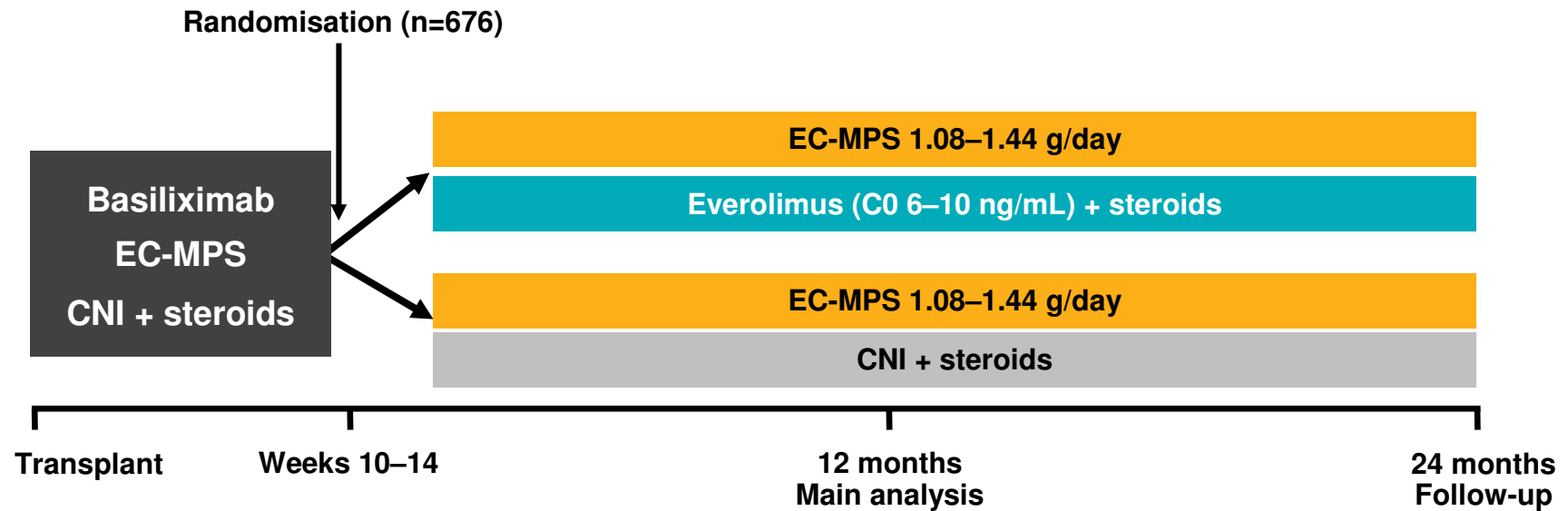
Time to first BPAR (ZEUS)



Conclusions

- **A rapid protocol conversion from cyclosporine to everolimus 7 weeks after renal transplantation significantly improved mGFR after one year both in the ITT- and the PP-population**
- **The everolimus arm showed:**
 - **A higher rate of discontinued study medication, mainly due to adverse events**
 - **A higher rate of rejections, which were mostly low grade and all treatable without graft losses**

ELEVATE is prospectively investigating LVH and PWV as secondary end points



Secondary end points: LVH assessed by LVMi and arterial stiffness assessed by PWV, at Month 12

Recruitment began in September 2010
LVH, left ventricular hypertrophy; PWV, pulse wave velocity;
EC-MPS, enteric-coated mycophenolate sodium;
CNI, calcineurin inhibitor; LVMi, left ventricular mass index

Off-label use

Material

292 - Kidney transplantations performed in 2009



- 71 with no biopsy at one year or recipient <18 years of age
- 9 with indication biopsies at one year

212



- 21 with indication biopsies at week 6

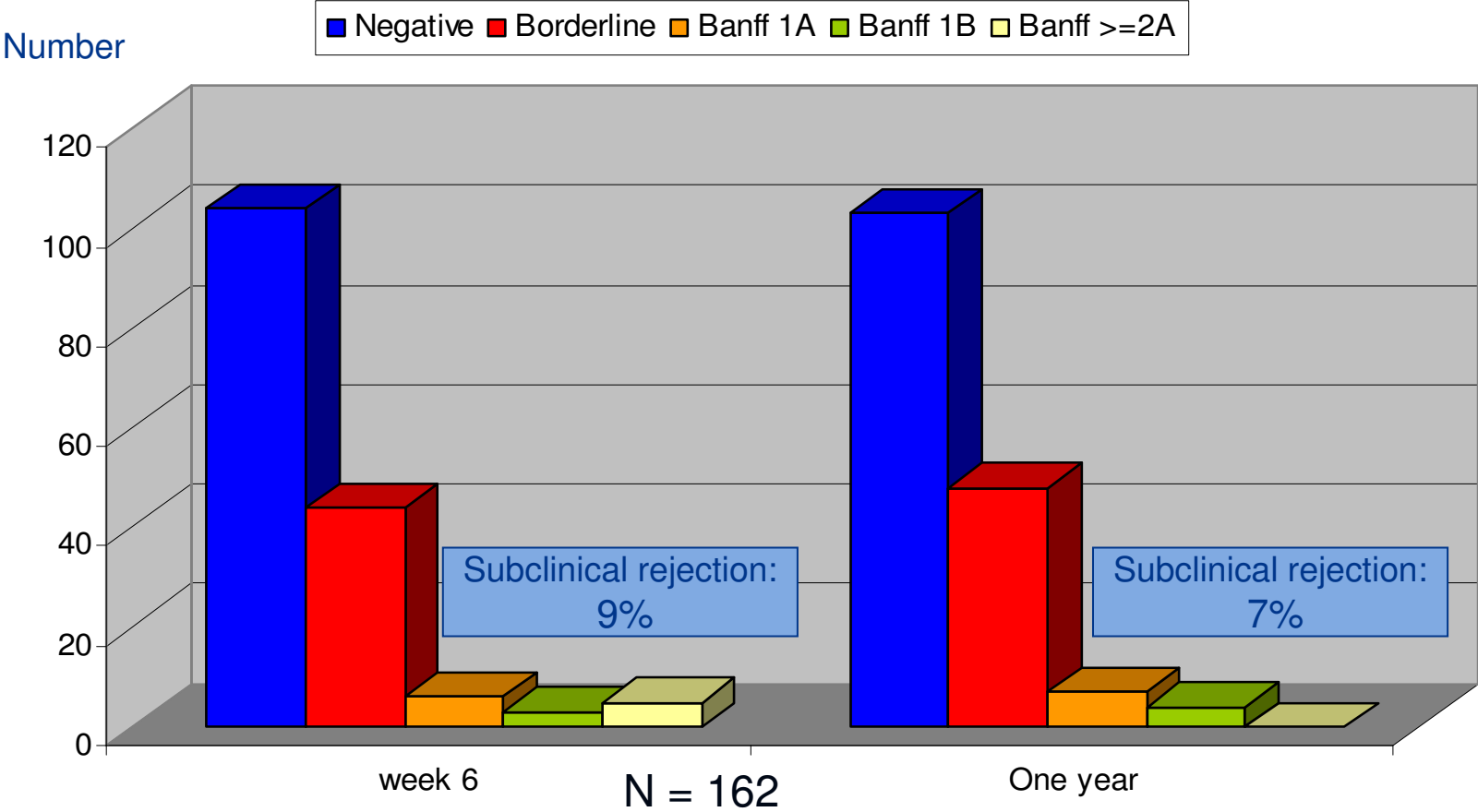
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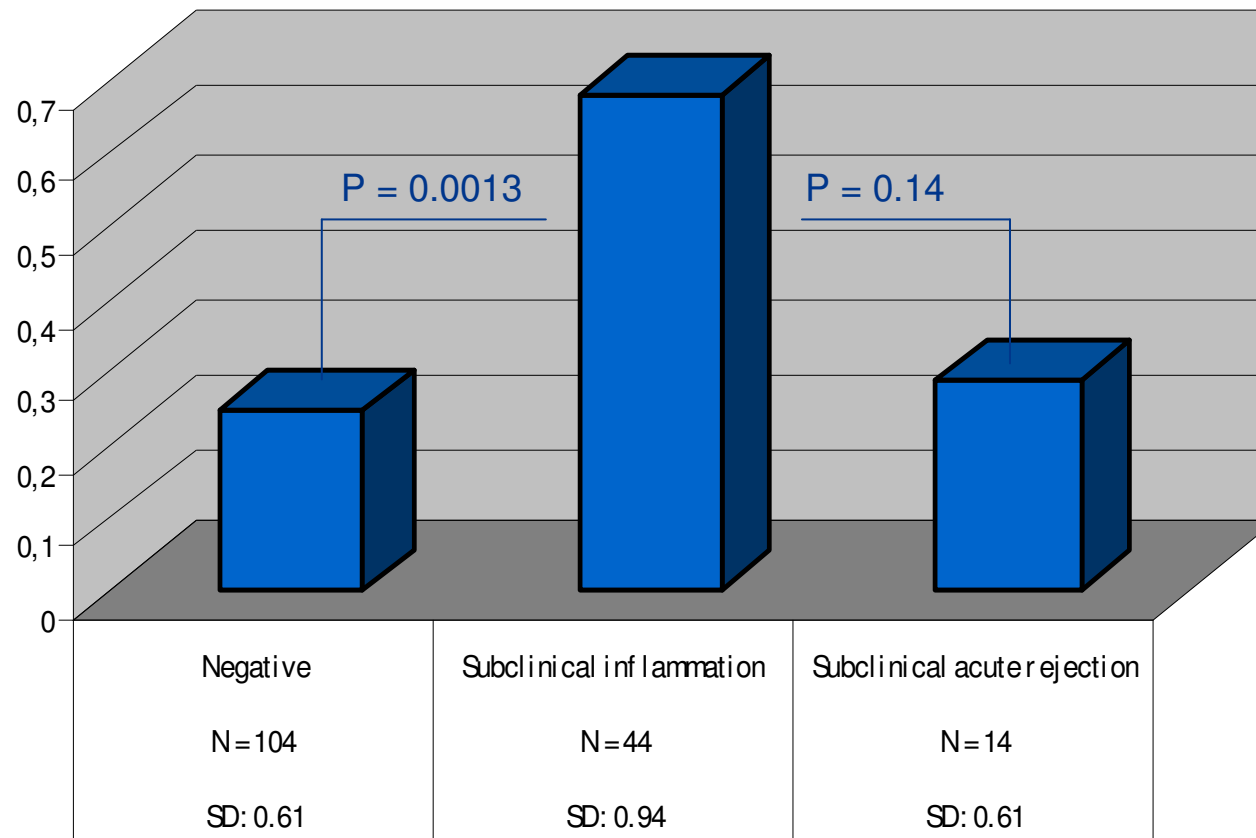
- 10 recipients with DSA
- 4 recipients with ABO incompatible transplantation
- 15 Combined Kidney and Pancreas

162 low risk recipients included in analysis

Protocol biopsies



Interstitial inflammation (i score) at one year according to Banff classification at week 6



Conclusions

- Subclinical rejection was evident in 9% of protocol biopsies at week 6 and 7 % at one year.
- Recipients with subclinical inflammation at week 6 had increased tubulitis (t) and interstitial (i) inflammation at one year
- Tubulointerstitial inflammation or treated subclinical rejection at week 6 did not predict increased fibrosis at one year .