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OBJECTIVES

Background: Renal impairment (RI) is a poor prognostic factor in multiple myeloma (MM). Analysis of disease characteristics, therapy & outcomes can improve treatment & prognosis.

Aims:

- To assess characteristics of patients with RI at diagnosis - severity of RI, age, risk factors, high risk features, stage, disease manifestations & performance status.
- To assess treatment including induction therapy & autologous stem cell transplant (ASCT) and outcomes.

METHODS

- Analysis of data from newly diagnosed MM patients enrolled in the Australian and New Zealand Myeloma Registry from 1 Feb 2013 to 31 Mar 2017.
- The KDIGO classification for chronic kidney disease (CKD) was used to classify renal function as recommended by the International Myeloma Working Group.
- In ASCT analyses, only patients with diagnosis date ≥ 1 year prior to data extraction are included (to allow time for transplant)

Table 1. Patient characteristics & therapy by renal function

Variable	eGFR <60 (n=302)	eGFR \geq 60 (n=541)	P-value
Age (median, years)	72 (63-79)	64 (56-70)	<0.001
Age group > 70 years	55% (167/302)	25% (137/541)	<0.001
International Staging System = 3	64% (139/218)	12% (47/402)	<0.001
High-risk group†	55% (166/302)	47% (256/541)	0.03
Lactate dehydrogenase, U/L	204 (159-262)	185 (154-235)	0.01
ECOG performance status (2-4)	28% (53/191)	19% (73/378)	0.02
Diabetes‡	13% (38/302)	7% (40/541)	0.01
Hypercalcaemia	12% (35/302)	4% (21/541)	<0.001
Anaemia	46% (138/302)	14% (78/541)	<0.001
Bone lesions	53% (161/302)	65% (349/541)	0.001
Bortezomib-based therapy	83% (224/269)	91% (430/475)	0.004
ASCT performed*	27% (49/179)	57% (194/343)	<0.001
Age \leq 70 & ASCT performed*	60% (48/80)	73% (191/262)	0.03
Serum creatinine, μ mol/L	146 (115-239)	76 (66-88)	
eGFR	37 (20-50)	83 (71-90)	
Best clinical response (\geq PR)	83% (144/174)	85% (296/349)	0.54
BCR: Bortezomib-based therapy (\geq PR)	88% (133/152)	87% (276/316)	0.96
Time from Dx to Rx (median, days)	14 (5-28)	24 (13-42)	<0.001
Time from Dx to ASCT (median, months)	5.7 (4.7-7.6)	6.5 (5.3- 8.2)	0.10
Time to disease progression (months)	28.5 (16.8-42.7)	30.1 (19.7-**)	0.18

†High risk classification based on FISH and LDH, **=75th percentile not available, ‡ diabetes requiring medication, *of patients with diagnosis date ≥ 1 year prior, PR=partial response

RESULTS: PATIENT CHARACTERISTICS

- Of 931 MM patients, 843 had eGFR available at diagnosis:
 - 36% (302/843) had eGFR < 60 ml/min: renal impairment (RI)
 - 30-60 ml/min: 23%; 15-30 ml/min: 6%; <15 ml/min: 7%
- Mean age was higher in patients with RI: 72 y in RI vs 64 y without RI ($p < 0.001$).
- Advanced stage (ISS III), anaemia and ECOG performance status of 2 to 4 (unable to work) were more prevalent in patients with RI.
- High-risk features of FISH (del 17p, t(4:14), t(14:16), amp1q21, del13q) and high LDH were also more prevalent in RI ($p \leq 0.03$, table 1)
- Diabetes mellitus (DM), a major cause of CKD, was more prevalent in patients with RI: 13% vs 7% ($p = 0.01$)
 - No impact of DM on disease response or survival
 - Patients with RI (<30 ml/min) and DM vs no DM had a
 - Similar response to first-line therapy (\geq PR, 77% vs 80%, $p = 0.83$)
 - No difference in OS (26 vs 37 mths, $p = 0.70$) or PFS (24 mths, $p = 0.72$).
- Bone lesions were less prevalent in RI (53% vs 65% $p = 0.001$).

RESULTS: THERAPY

- A lower proportion of patients with RI underwent ASCT (27% v 57%, $p < 0.001$, Table 1).
- Most patients (88%) received bortezomib-based therapy as first line, but this was less likely in those with RI (83% RI vs 91% no RI, $p < 0.004$).

RESULTS: RESPONSE RATES & SURVIVAL

- Responses of \geq PR for first-line therapy were the same in patients with eGFR <60 ml/min compared with normal renal function (83% vs 85%, $p = 0.54$). (see Fig. 1).
- TTP & OS decreased with reduction in eGFR (Fig. 2 and 3)
- Patients with eGFR ≥ 60 ml/min had a longer OS (HR 0.46, 95%CI 0.30-0.71, $p = 0.001$) compared with eGFR < 60 ml/min.

RESULTS: ASCT & OUTCOMES

- Using age 70y as a common age limit for ASCT, the effect of ASCT in patients <70y with and without RI was analysed:
- ASCT was performed at all levels of renal function; eGFR<15: 65%, 15-29: 40%, 30-59: 65%, 60-89: 70%, ≥ 90 : 77%.
- Fewer patients with RI received ASCT (60% vs 73%, $p < 0.03$)
- In patients with eGFR < 60 ml/min, those who received ASCT had a longer TTP (HR 0.41, 95%CI 0.17-0.96, $p = 0.04$) & OS (HR 0.30, 95%CI 0.08-1.05, $p = 0.06$) compared with no ASCT.
- Improvement in survival was also seen in severe RI (<30 ml/min), with a longer TTP (HR 0.21, 95%CI 0.05-0.86, $p = 0.03$) & OS (HR 0.10, 95%CI 0.01-0.82, $p = 0.03$) with ASCT.
- There was no difference in TTP (HR 1.06, 95%CI 0.57-1.97, $p = 0.86$ (NS)) & OS (HR 0.89, 95%CI 0.29-2.79, $p = 0.85$ (NS)) between patients with & without RI who undergo ASCT.

Figure 1. Best clinical response to first-line therapy in patients with and without RI

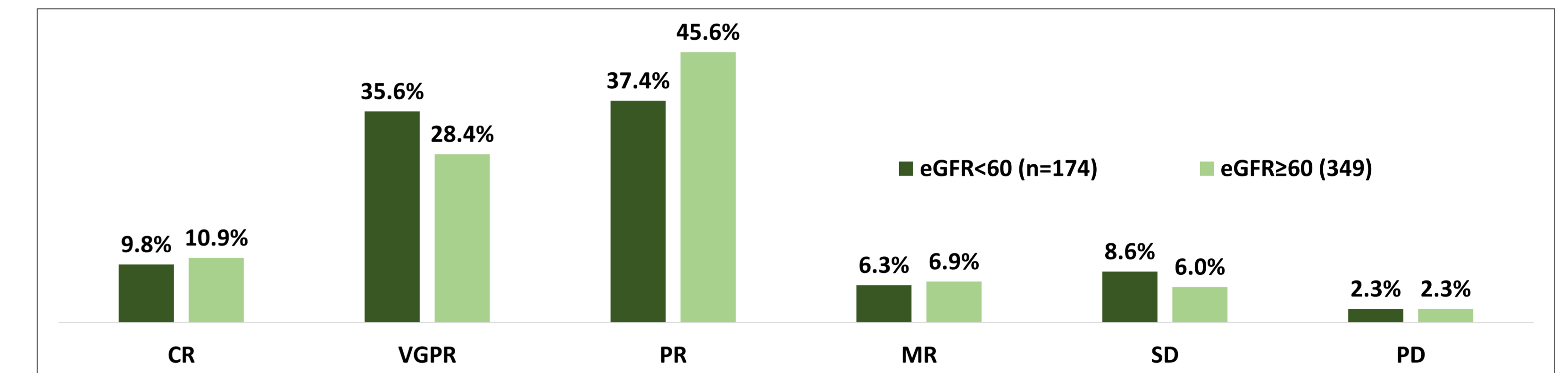


Figure 2. Time to progression (TTP) by renal function grouping

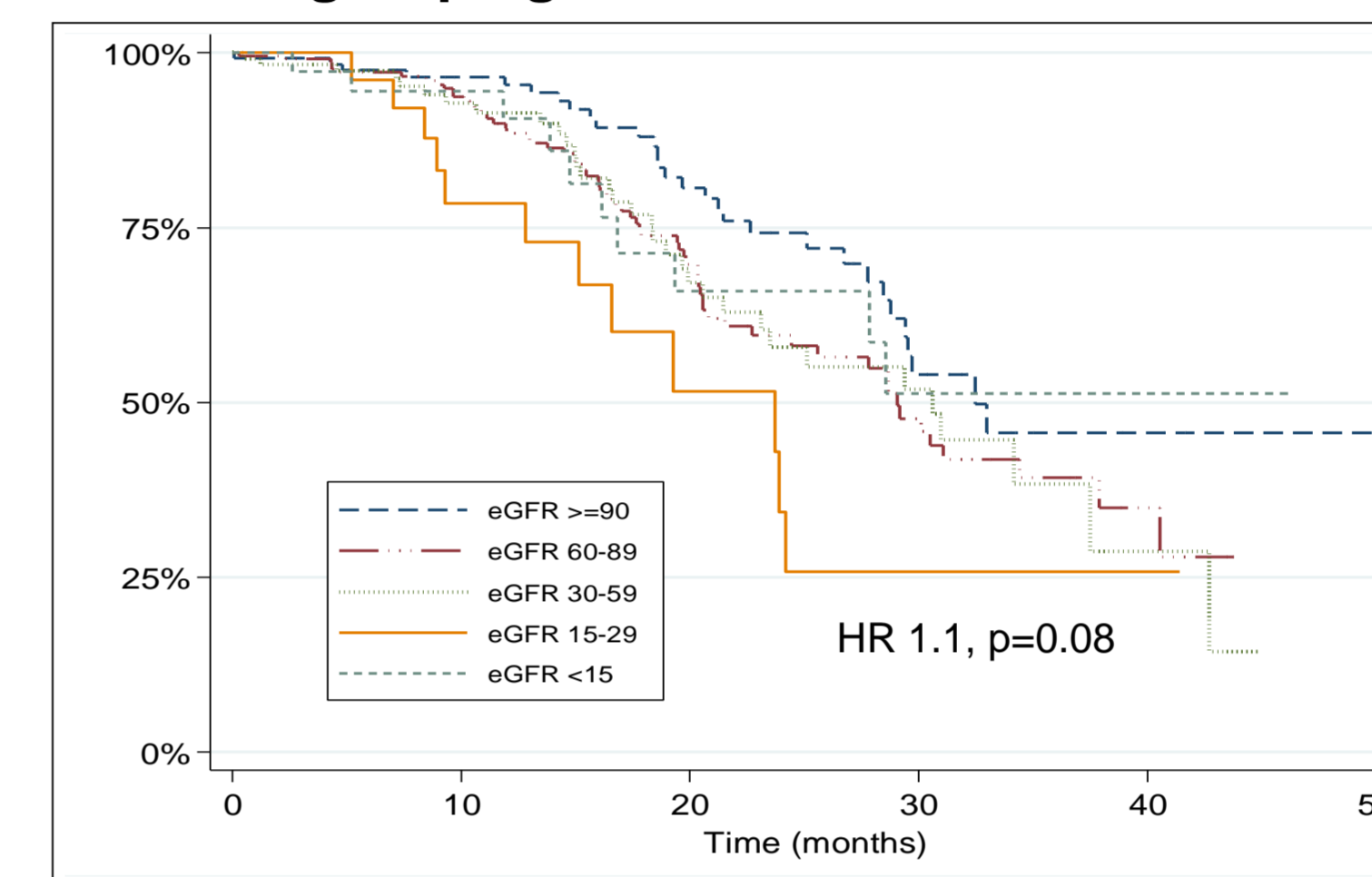


Figure 3. Overall survival (OS) by renal function grouping

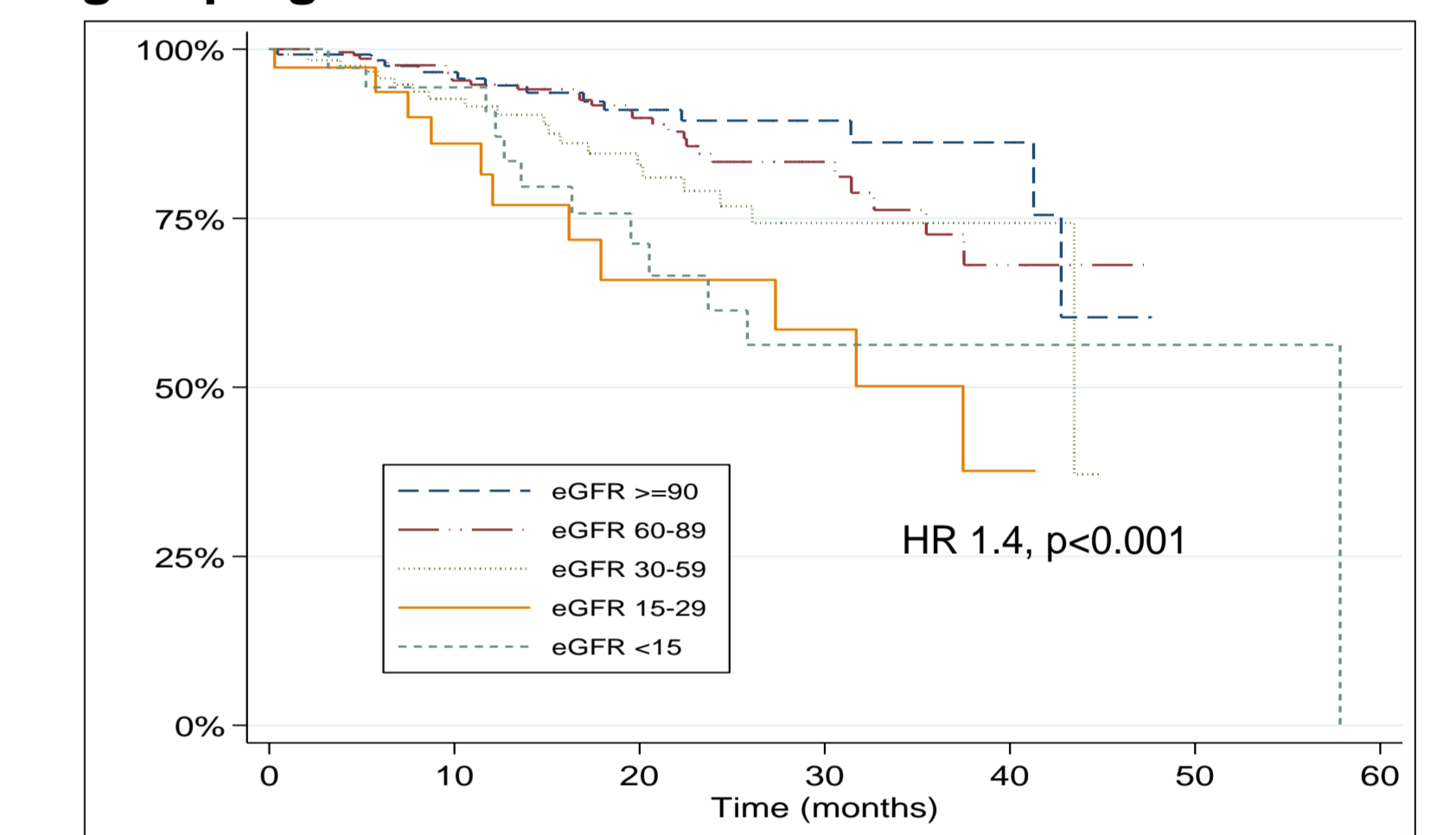


Figure 4 (a) TTP and (b) OS in patients with eGFR <60 ml/min with and without ASCT

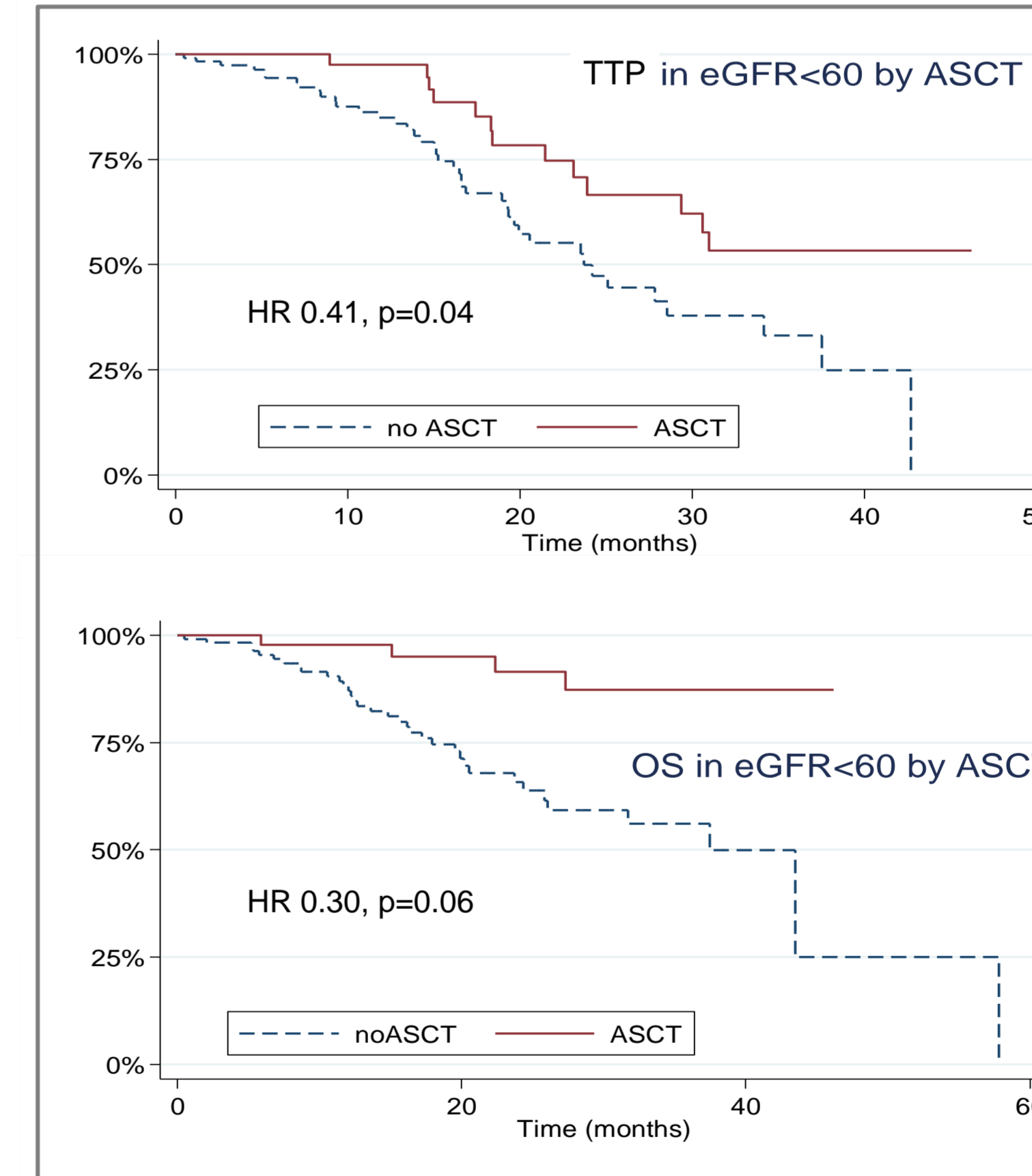
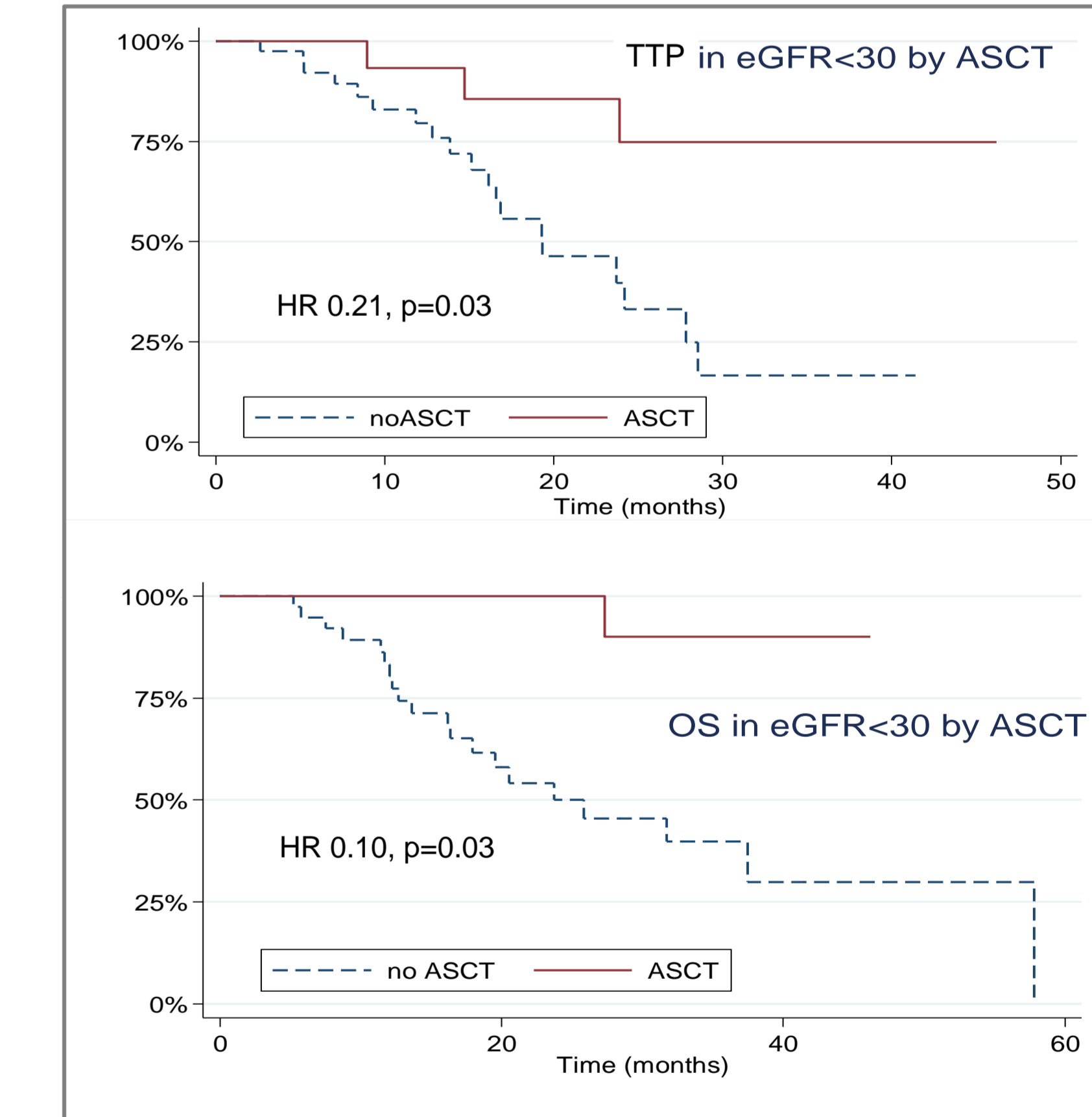


Figure 5 (a) TTP and (b) OS in patients with eGFR <30 ml/min with and without ASCT



CONCLUSIONS

- RI occurred in one-third of newly diagnosed MM.
- DM was more common in RI, but not associated with difference in outcome.
- Advanced stage & high risk features were more prevalent in RI.
- Bone disease was less common.
- RI patients had a shorter OS, correlating with eGFR.
- In transplant-eligible patients assessed by age <70y, ASCT was performed in 60% of RI patients, at all levels of renal function.
- Patients with RI who underwent ASCT had a superior TTP and OS than those who did not have ASCT, including those with severe RI (eGFR <30 ml/min), supporting the benefit of ASCT in MM patients with RI.