Blood Neutrophil-to-Lymphocyte Ratio Predicts Survival in Patients with Malignant Mesothelioma

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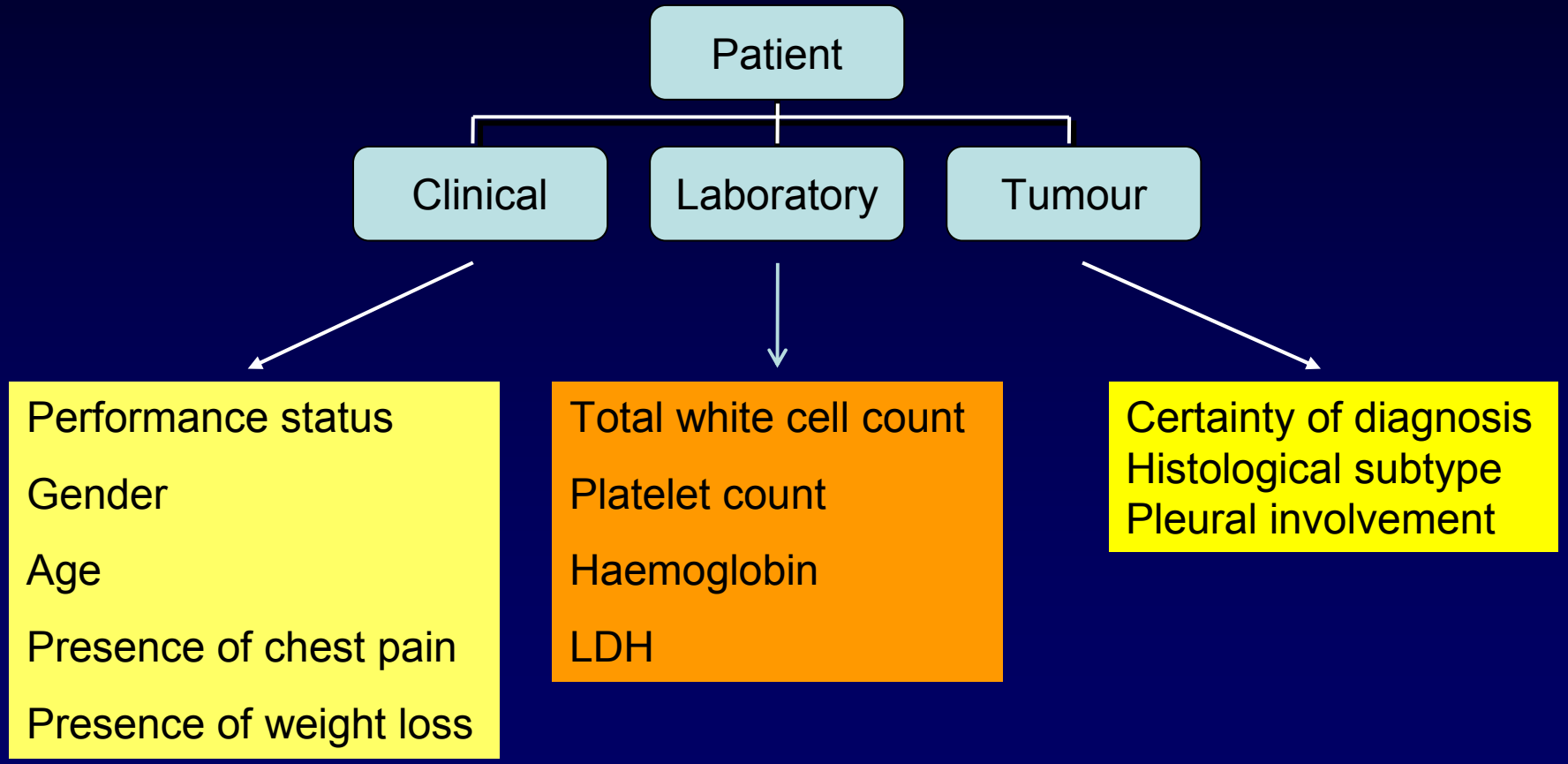
Malignant Mesothelioma (MM)

- Epidemiology
  - in Australia – no longer rare
  - in developing countries – a time bomb
- Current standard 1st line therapy for MM = cisplatin + pemetrexed
  - median survival 12 months
  - response rate ~40%
- Staging in MM difficult
  - accurate, reliable and easily accessible predictors of chemotherapy response and survival are needed to guide clinical decision-making.

Validated Prognostic Factors



Neutrophil-to-Lymphocyte Ratio (NLR)

- NLR = absolute neutrophil ÷ absolute lymphocyte
- Inflammation based score
  - relative neutrophilia + lymphocytopenia
- High NLR (≥ 5) - adverse prognosis in
  - heart disease
  - some cancers

NLR predicts survival in patients with colorectal cancer liver metastases

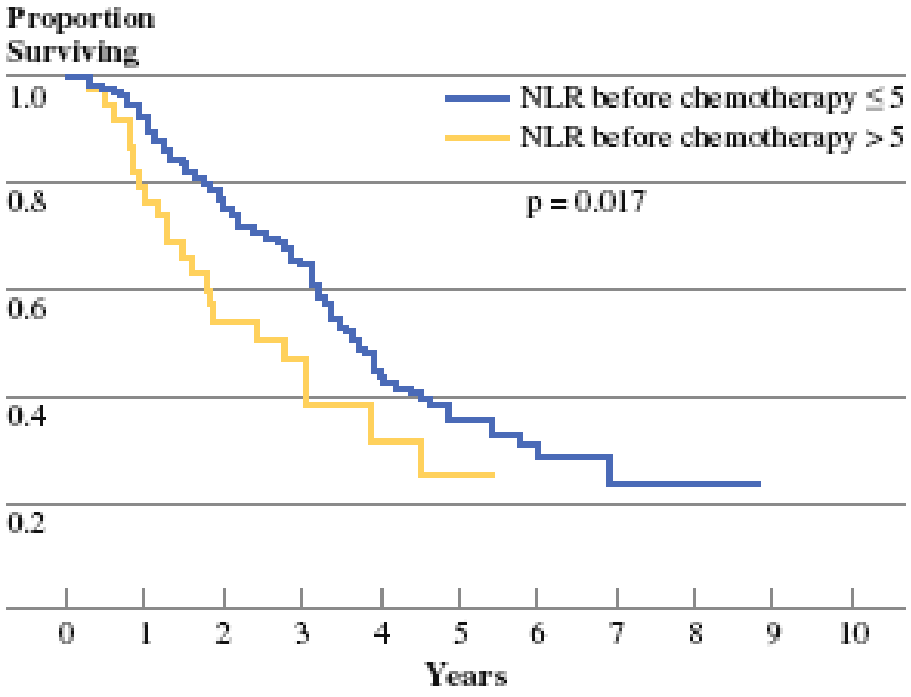


FIG. 1 Survival of all patients according to NLR before chemotherapy

n= 290 prior to liver resection

Kishi et al (2009) Ann Surg Oncol

Research Question

Is blood NLR a useful prognostic tool for MM patients undergoing chemotherapy?

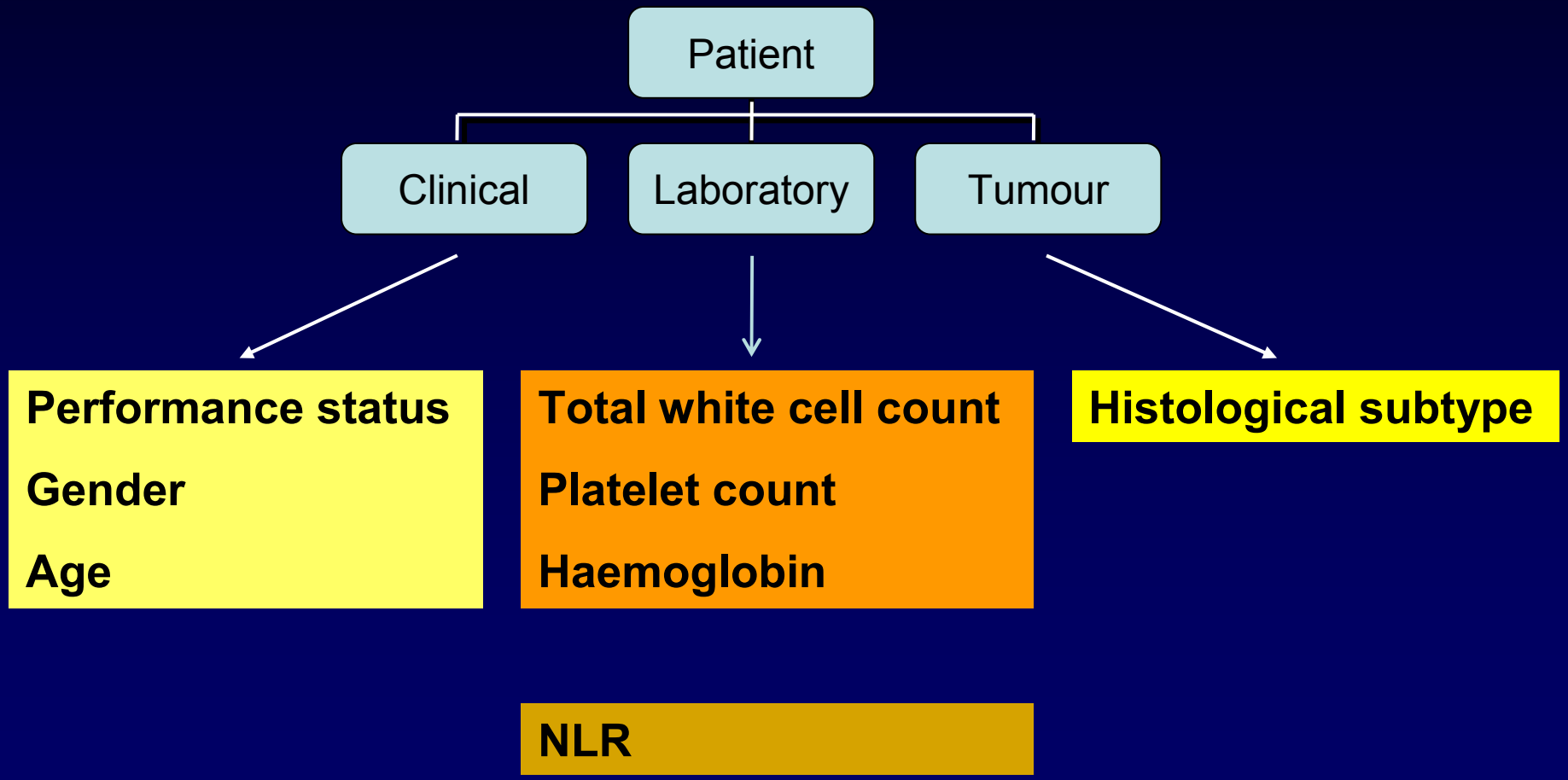
Hypothesis:

- Patients with high NLR prior to commencement of chemotherapy will do worse in terms of
  - overall survival
  - response rate

Methods

- Retrospective chart review
- MM patients who had pemetrexed-based chemotherapy from 2004 to 2009 at Sydney Cancer Centre

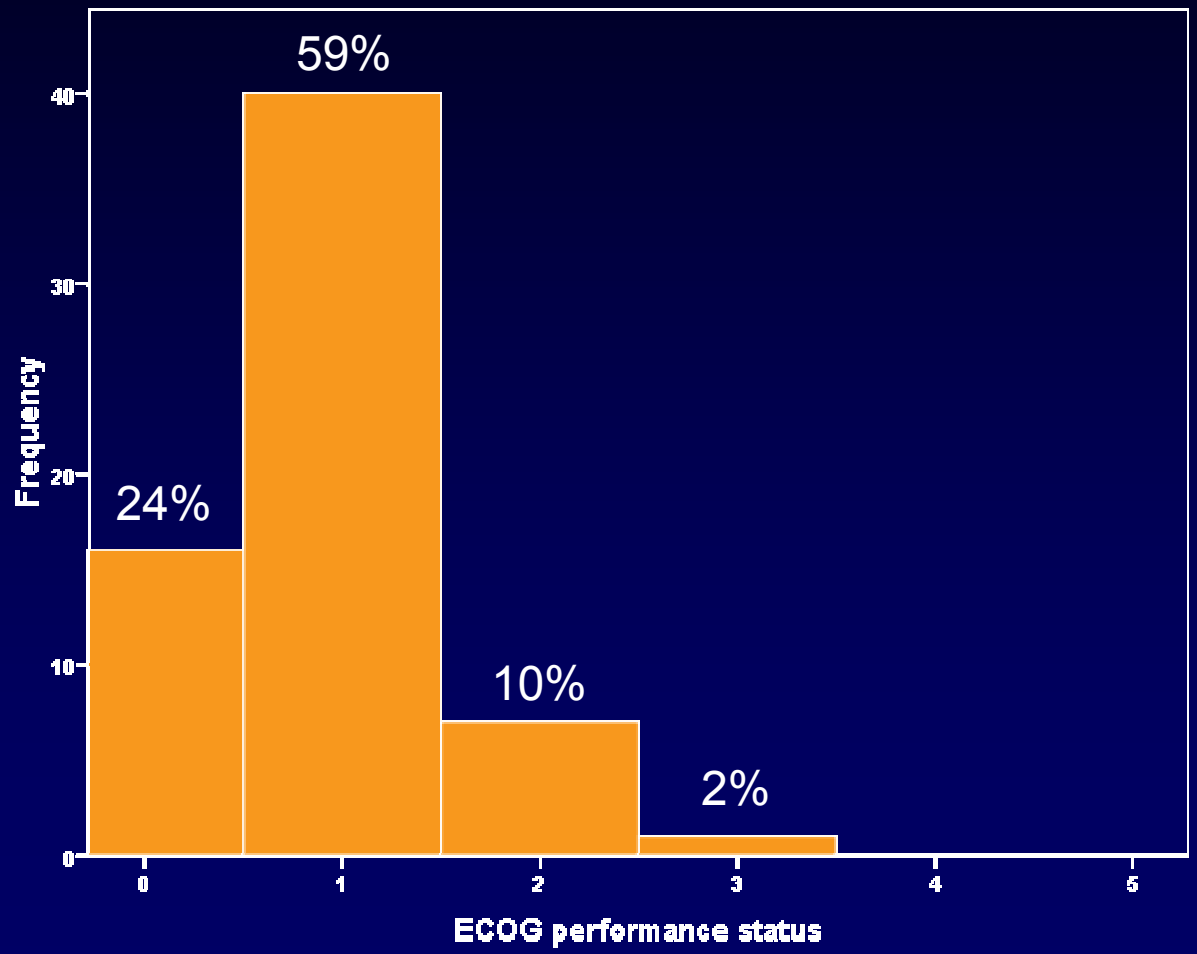
Potential Predictors Examined



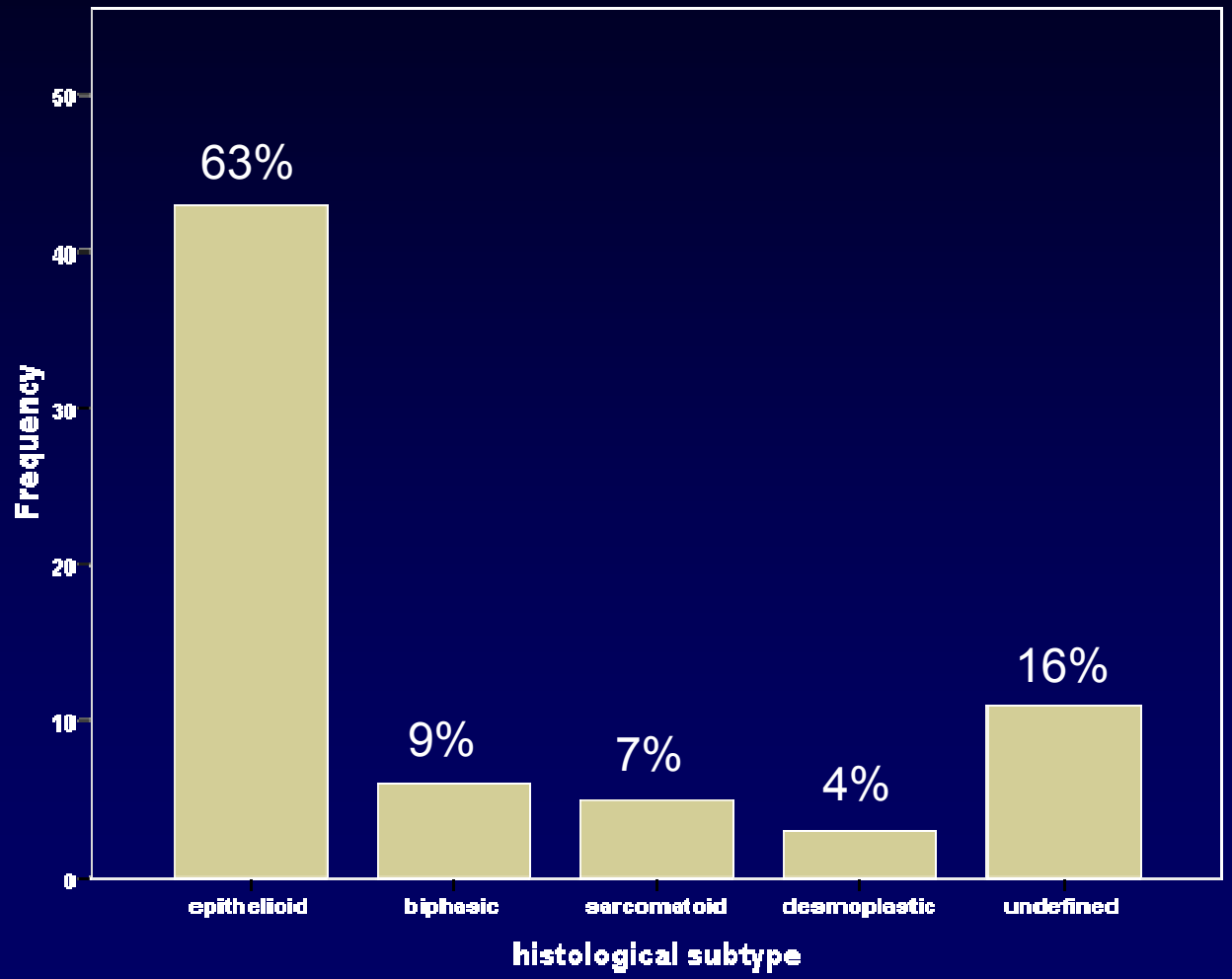
Results

- 68 patients identified
- Median age: 62 years (range 41-82)
- Gender:
  - male 82%
  - female 18%

Performance Status



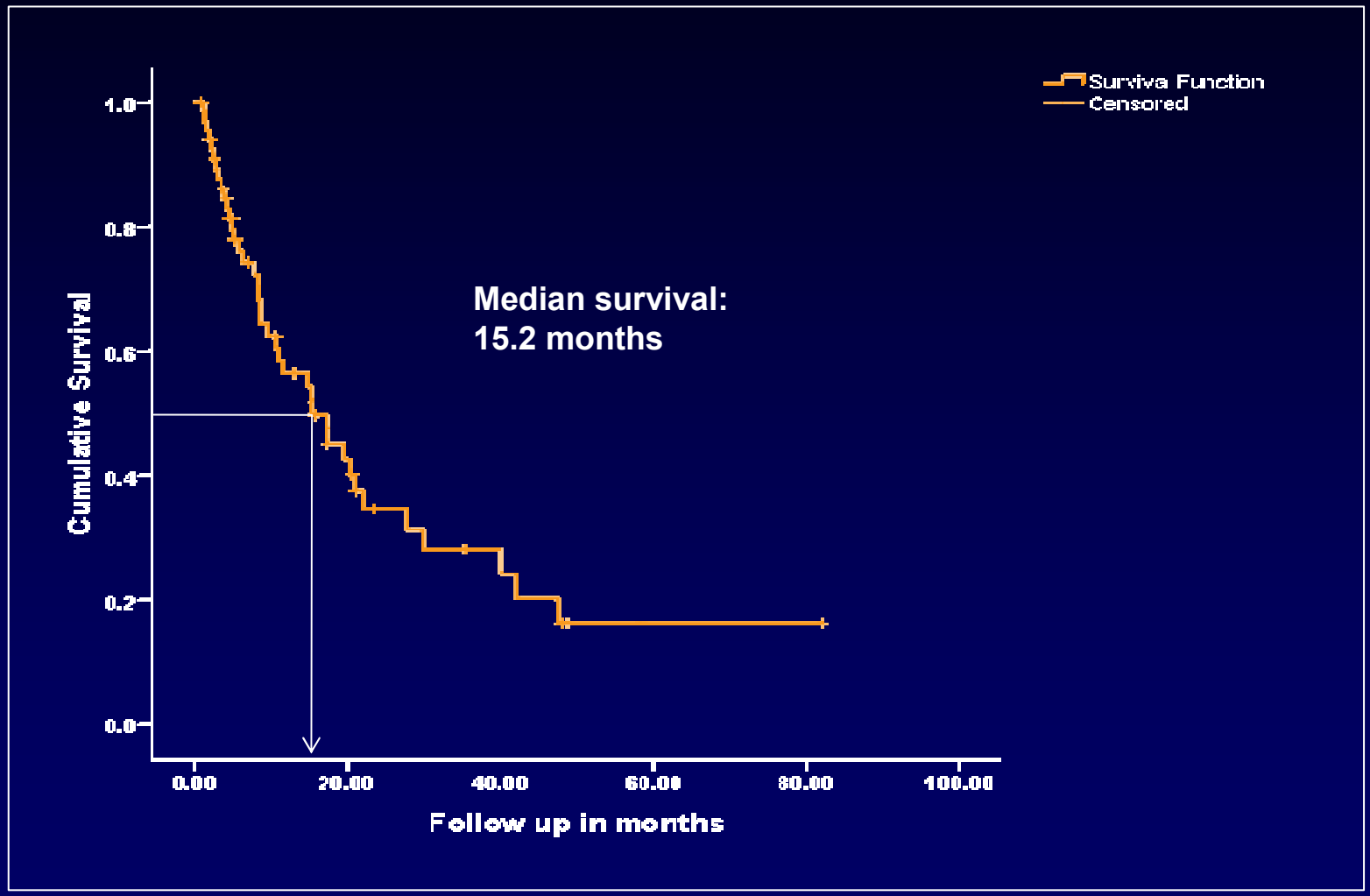
Histological subtype



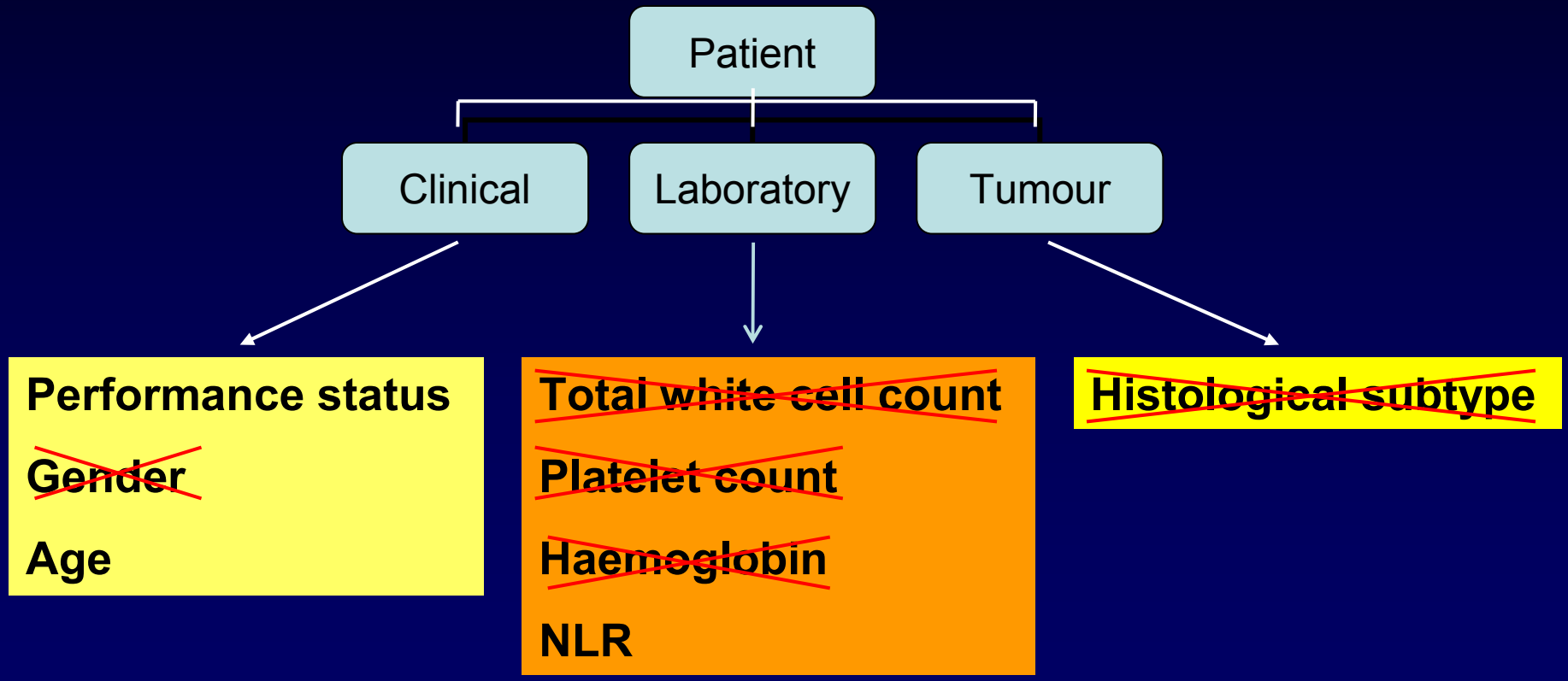
- The median number of chemotherapy cycles administered was 5 (range 1-16)

- Median follow up = 14.5 months
- At the time of report, 57% of patients were deceased.

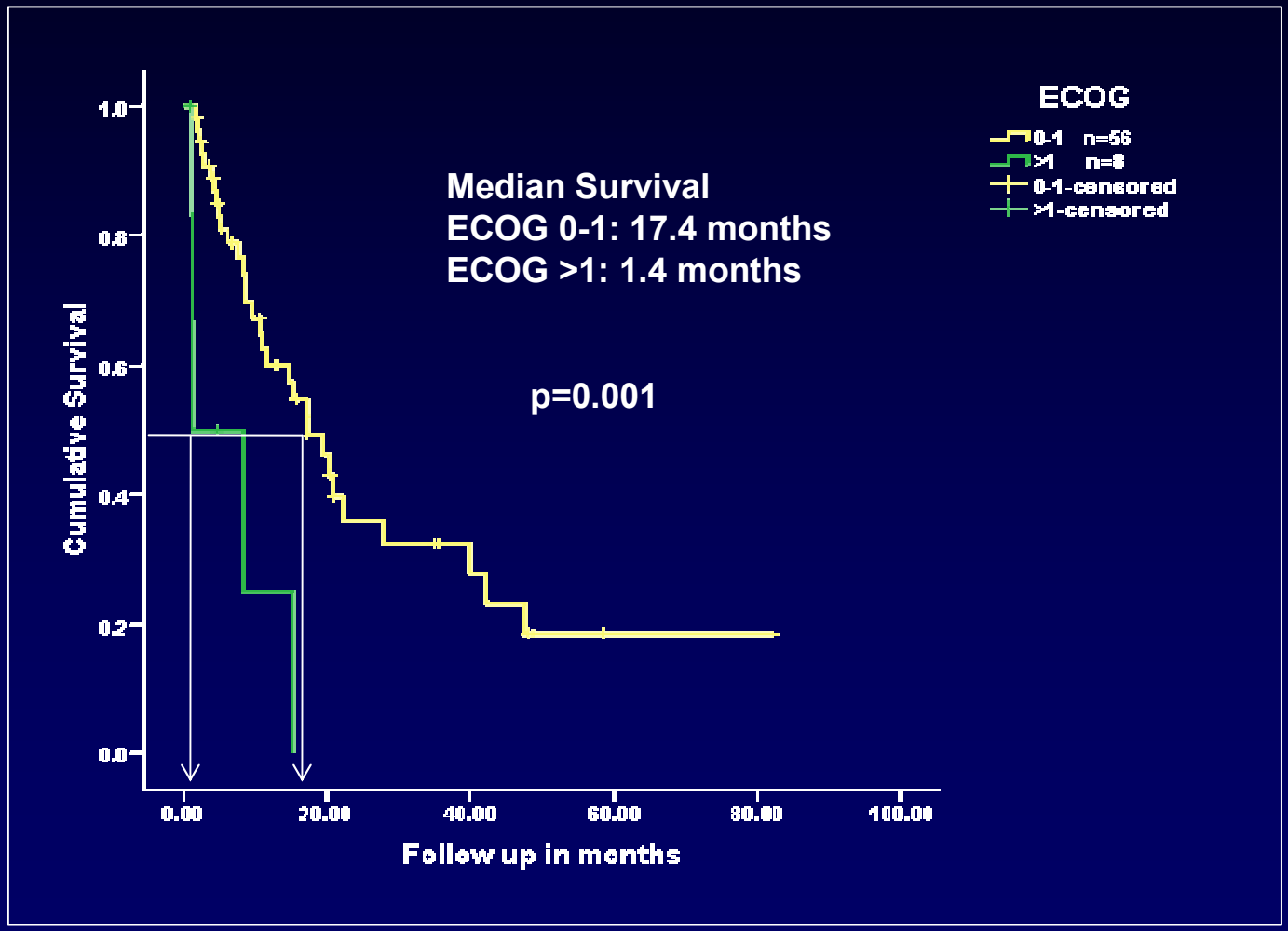
Overall Survival



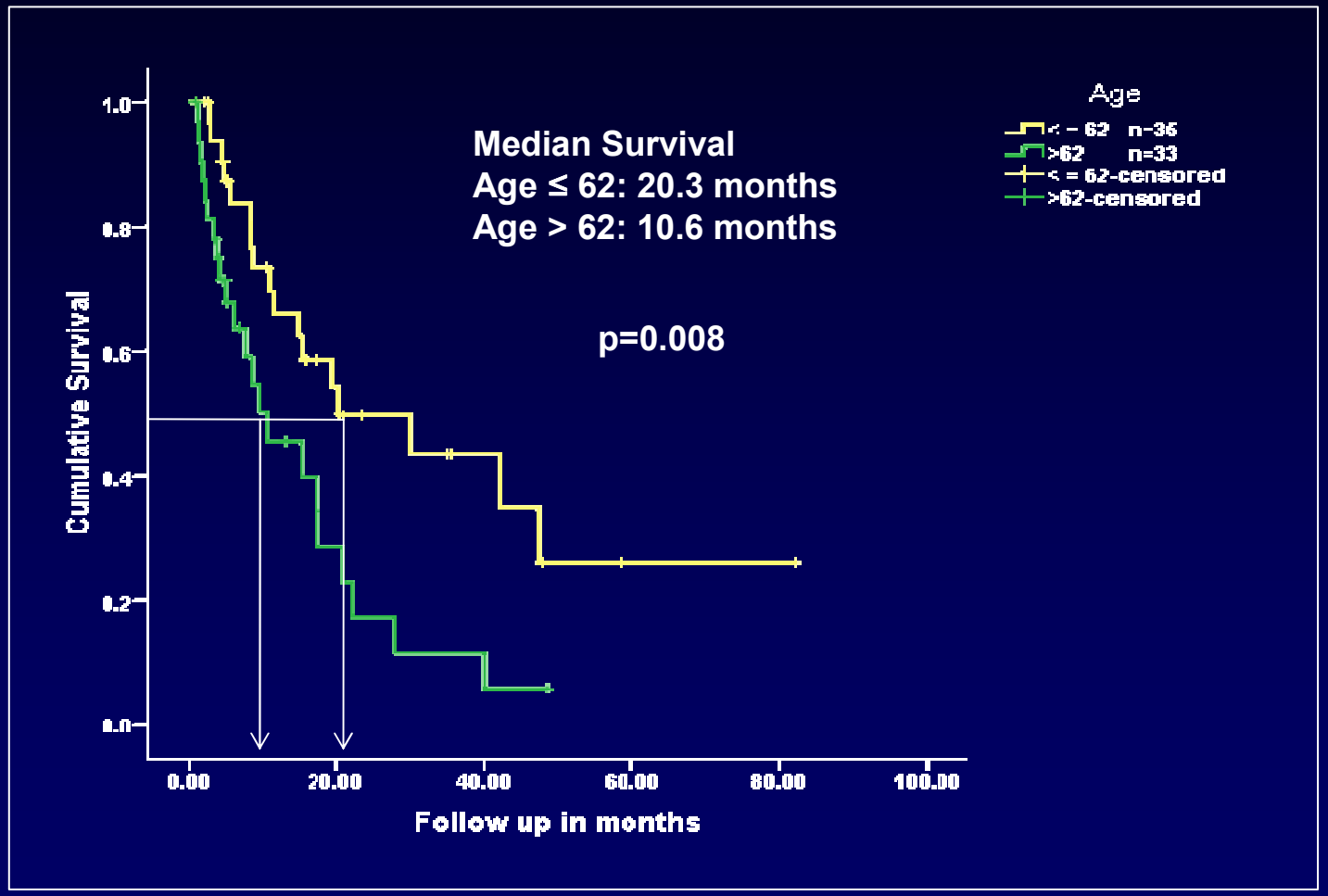
Predictors for Survival univariate analysis



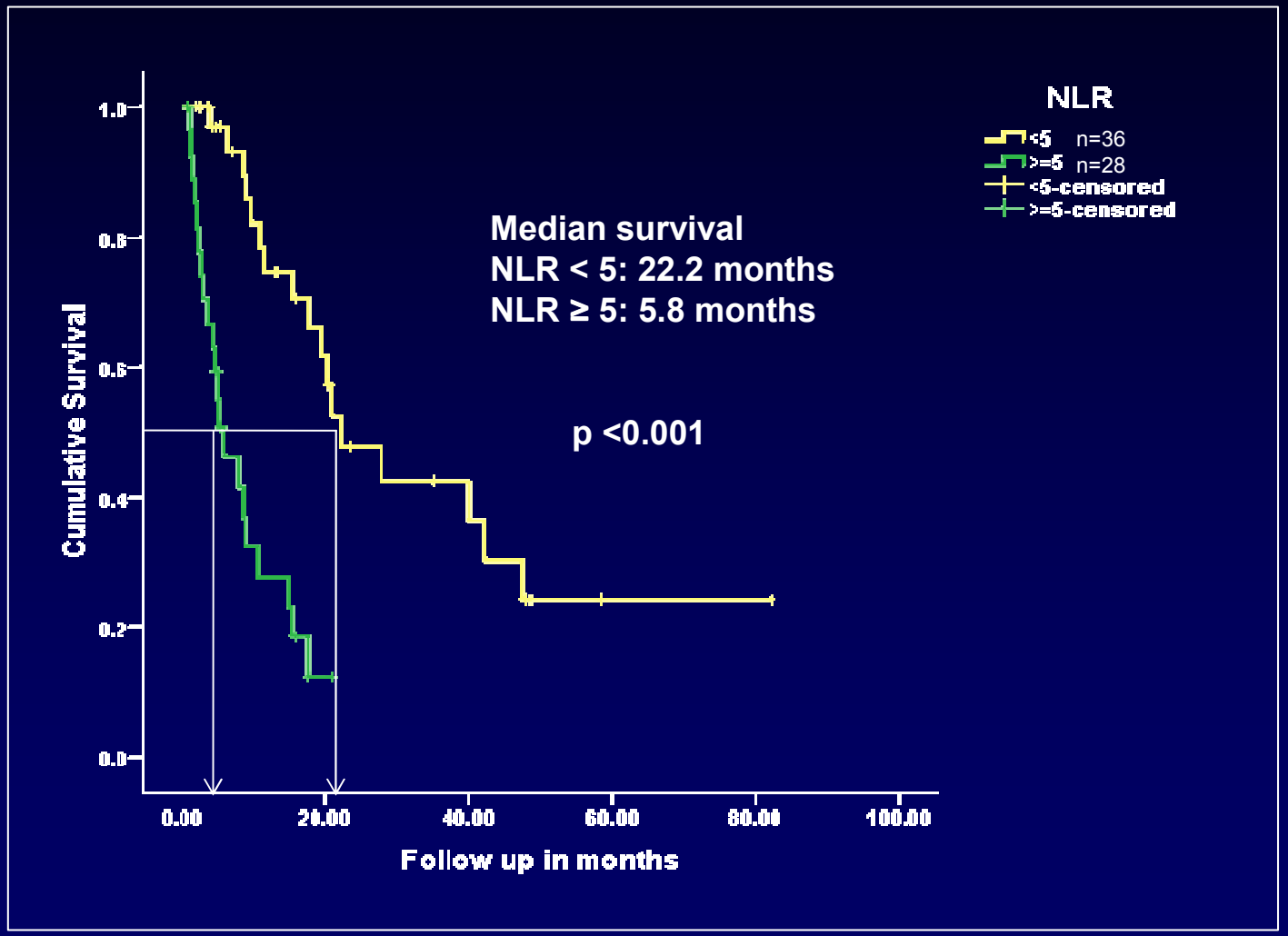
Performance Status



Age


Median Survival
Age ≤ 62: 20.3 months
Age > 62: 10.6 months
p=0.008
Age
<= 62 n=36
>62 n=33
<= 62-censored
>62-censored
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0.00
20.00
40.00
60.00
80.00
100.00
Follow up in months

NLR


NLR
<5 n=36
>=5 n=28
<5-censored
>=5-censored
Median survival
NLR < 5: 22.2 months
NLR ≥ 5: 5.8 months
p <0.001
Cumulative Survival
1.0
0.8
0.6
0.4
0.2
0.0
0.00
20.00
40.00
60.00
80.00
100.00
Follow up in months

Multivariate Analysis

Variables	n	No of event	Median Survival (months)	HR	95% CI	p value
Age (years)						
≤ 62	35	17	20.3	3.21	1.20-4.49	0.01
> 62	35	22	10.6			
Neutrophil-to-lymphocyte ratio						
<5	36	17	22.2	5.4	2.53-11.55	<0.001
≥5	32	21	5.8			

Response Rate

• Complete response	4%	Responders
• Partial response	30%	
• Stable disease	35%	Non-responders
• Progressive disease	22%	
• No measurable disease	2%	
• Unknown	7%	

Predictor for Response

NLR	Response to Chemotherapy			
	Yes	No	% yes	*p* value
< 5	16	17	48	0.025
≥ 5	5	20	20	

Conclusions

- Low NLR and younger age are independent predictors for better survival for patients with MM undergoing chemotherapy.
- 16 months difference in survival between high and low NLR is clinically significant.
- Low NLR is a predictor for chemotherapy response

Limitations

- Retrospective nature
  - results hypothesis generating
- Small sample size
- Variability of absolute differential white cell count
  - steroid

Implications

- Given the low cost of a white cell count, its easy reproducibility and wide accessibility, NLR is a potentially useful biomarker to predict outcome of patients undergoing chemotherapy.

- Future studies
  - Validation in other MM cohorts
  - Risk algorithm based on clinical and laboratory variables including NLR

Acknowledgement

- Jenny Peat for biostatistician support