

Management of The Neck After Primary Chemoradiation in Head and Neck Squamous Cell Carcinoma

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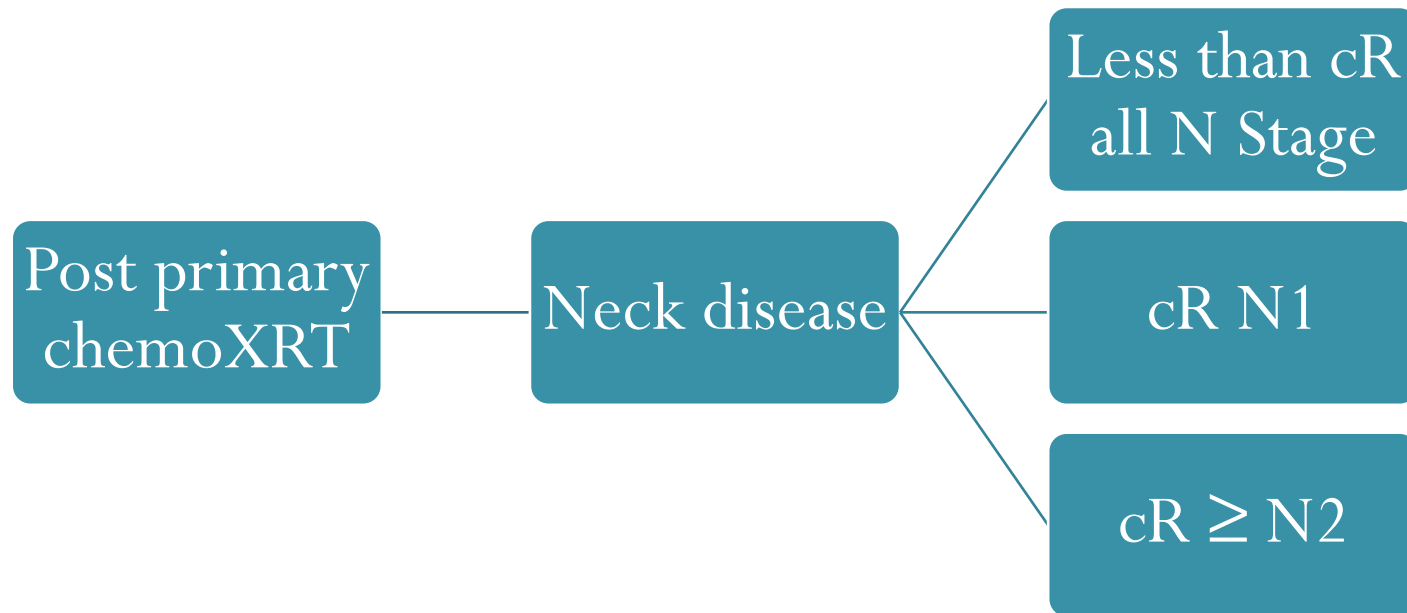
Needs assessment

- The current regimen at GBMC is for planned neck dissection (ND) post primary chemoradiation (chemoXRT) for head and neck squamous cell cancer (HNSCC) with $\geq N2$ neck disease. However there is a body of evidence suggesting observation for those patients with a complete response

Learner objectives

- Examine the need for planned ND post primary chemoXRT for \geq N2 neck disease with a complete response (cR)
- Evaluate the optimal timing of ND/imaging
- Examine the mode of monitoring response of the neck disease

Background



Background

Planned ND

- In \geq N2 disease
- To reduce regional recurrence
- Historically low response rate to fractionated radiation therapy alone
- Salvage of neck failure is poor
- Ideally performed 4 to 12 weeks after chemoXRT


Background

Why do we perform planned ND ?

- Lower radiation dose to uninvolved nodes in the neck
- Concern for micrometastases

Current Treatment paradigm

IMRT – 7000 to 7500 cGy to primary site.



IMRT – 6000 cGy to involved nodes



IMRT – 5000cGy to uninvolved nodes

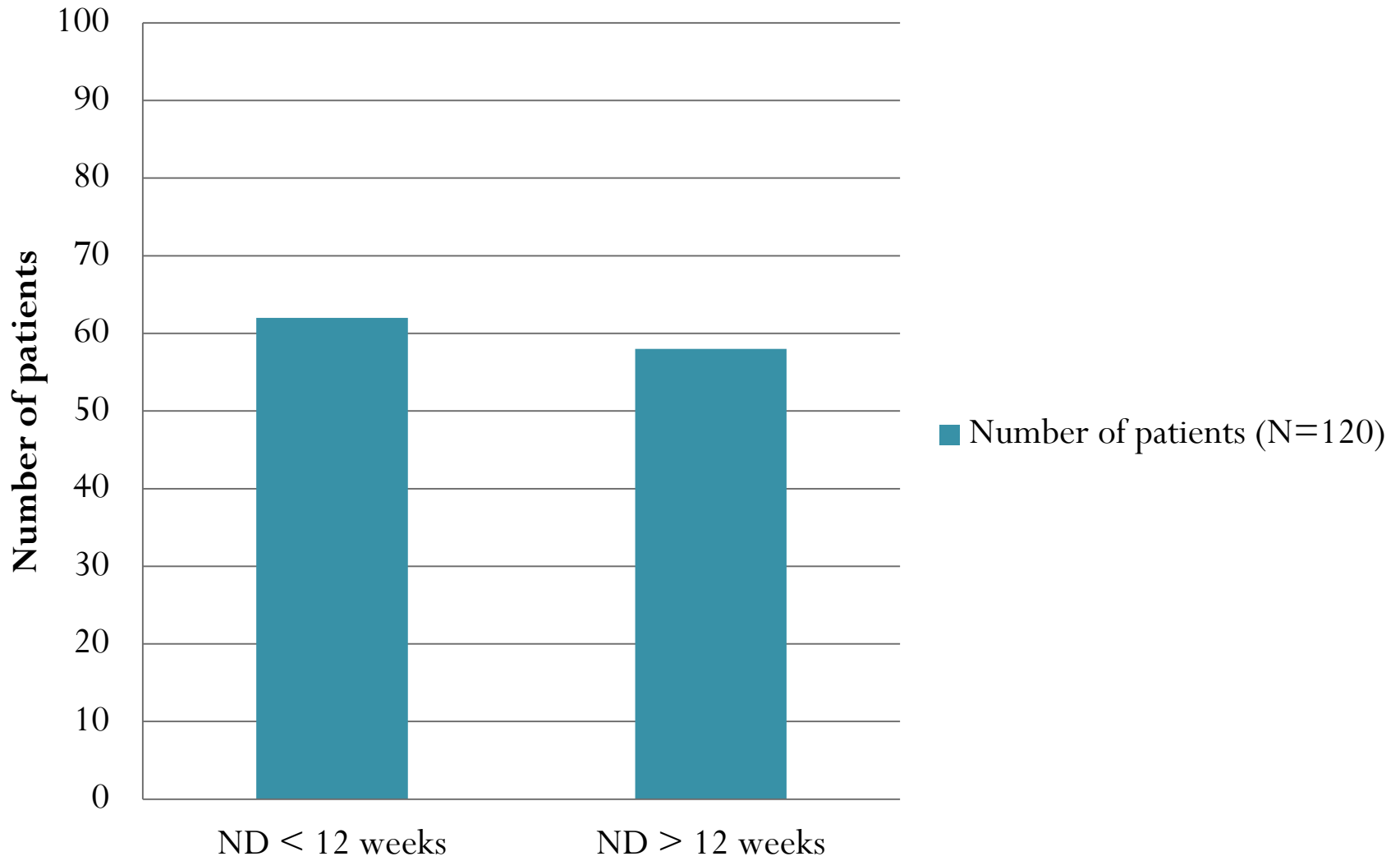


Concomitant cisplatin ($30\text{mg}/\text{m}^2$) weekly for 6 to 7 cycles

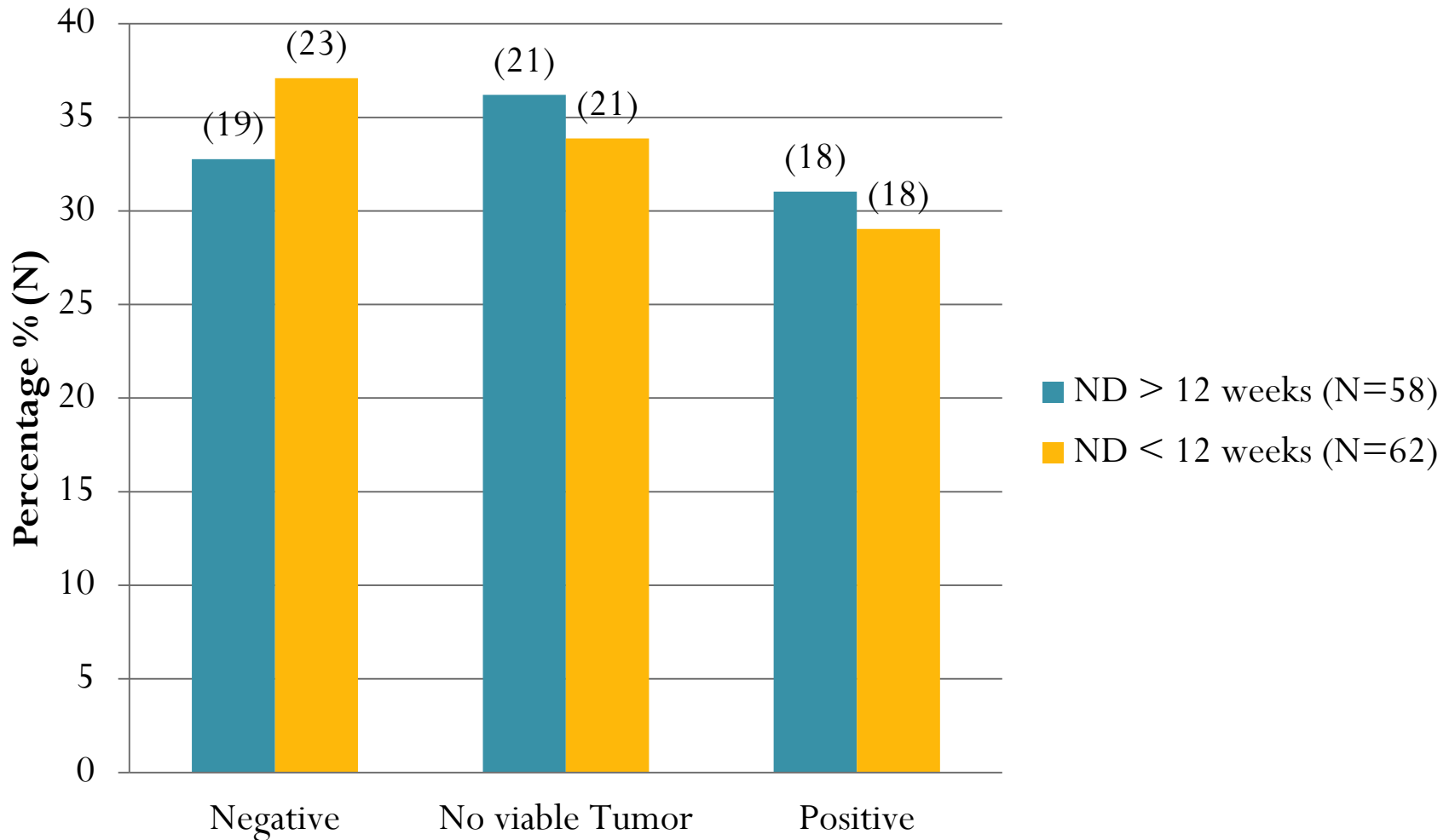


Planned neck dissection

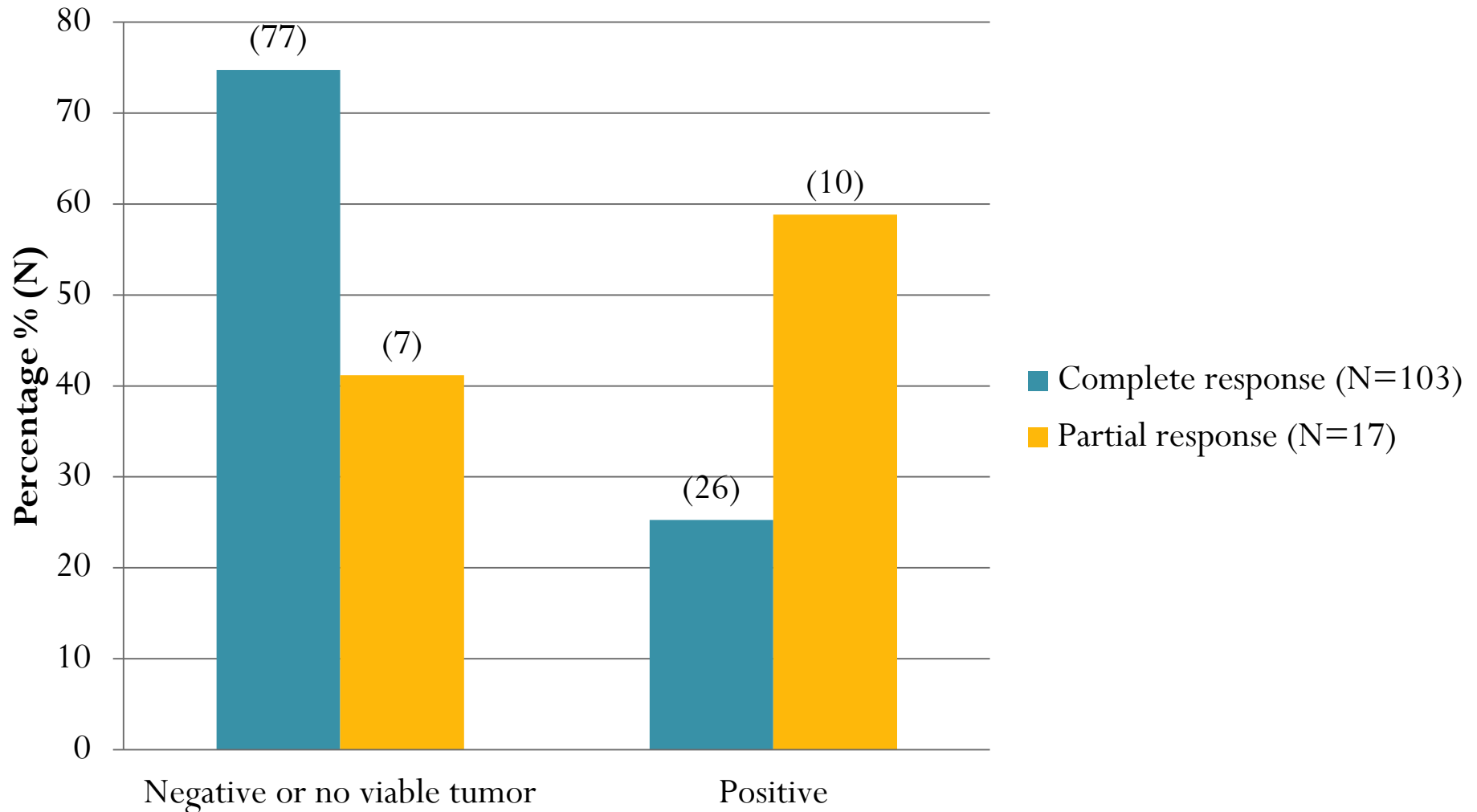
Planned Neck Dissections from 1999-2011



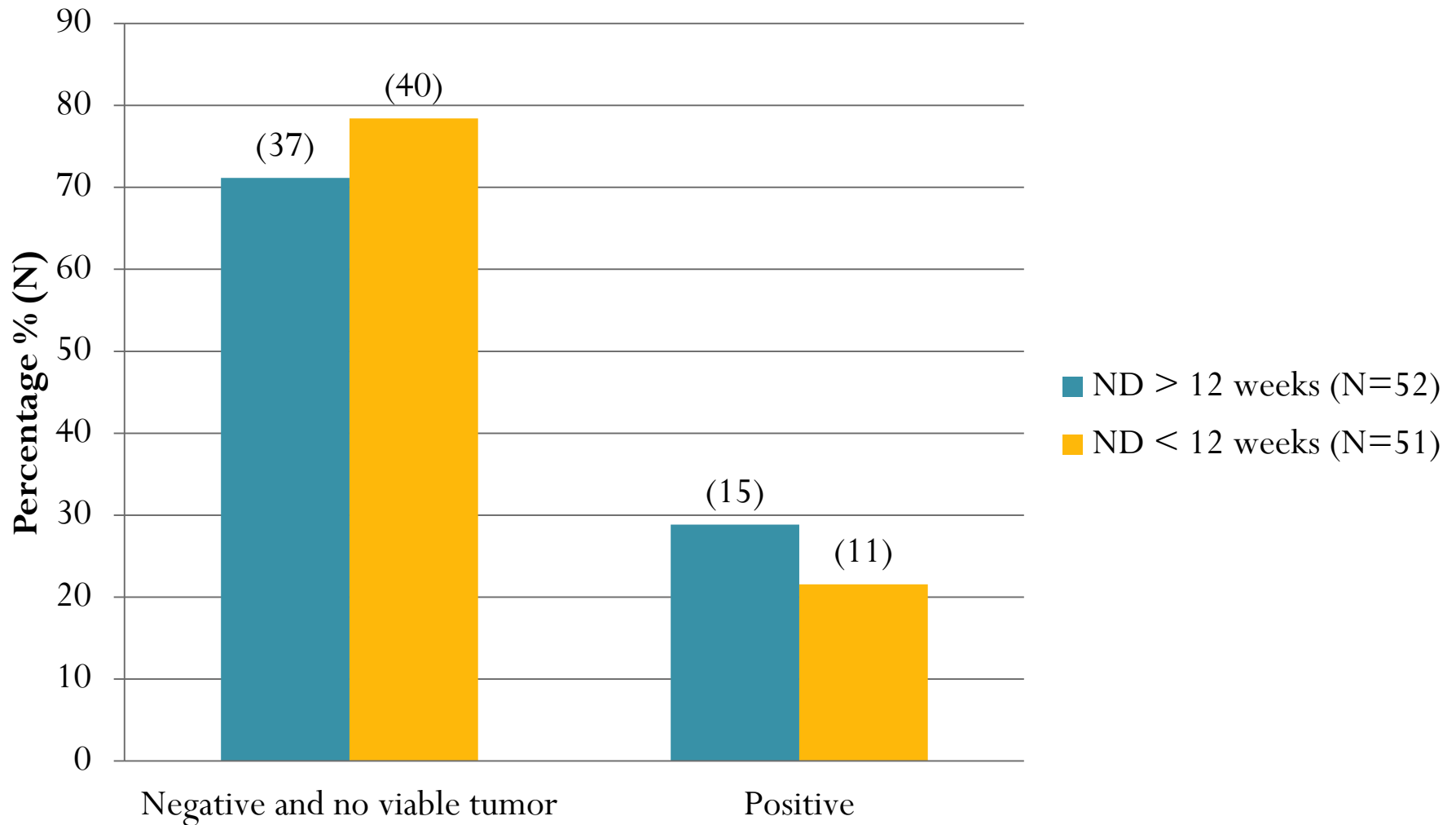
Pathological findings in specimens for neck dissections depending on timing (N=120)



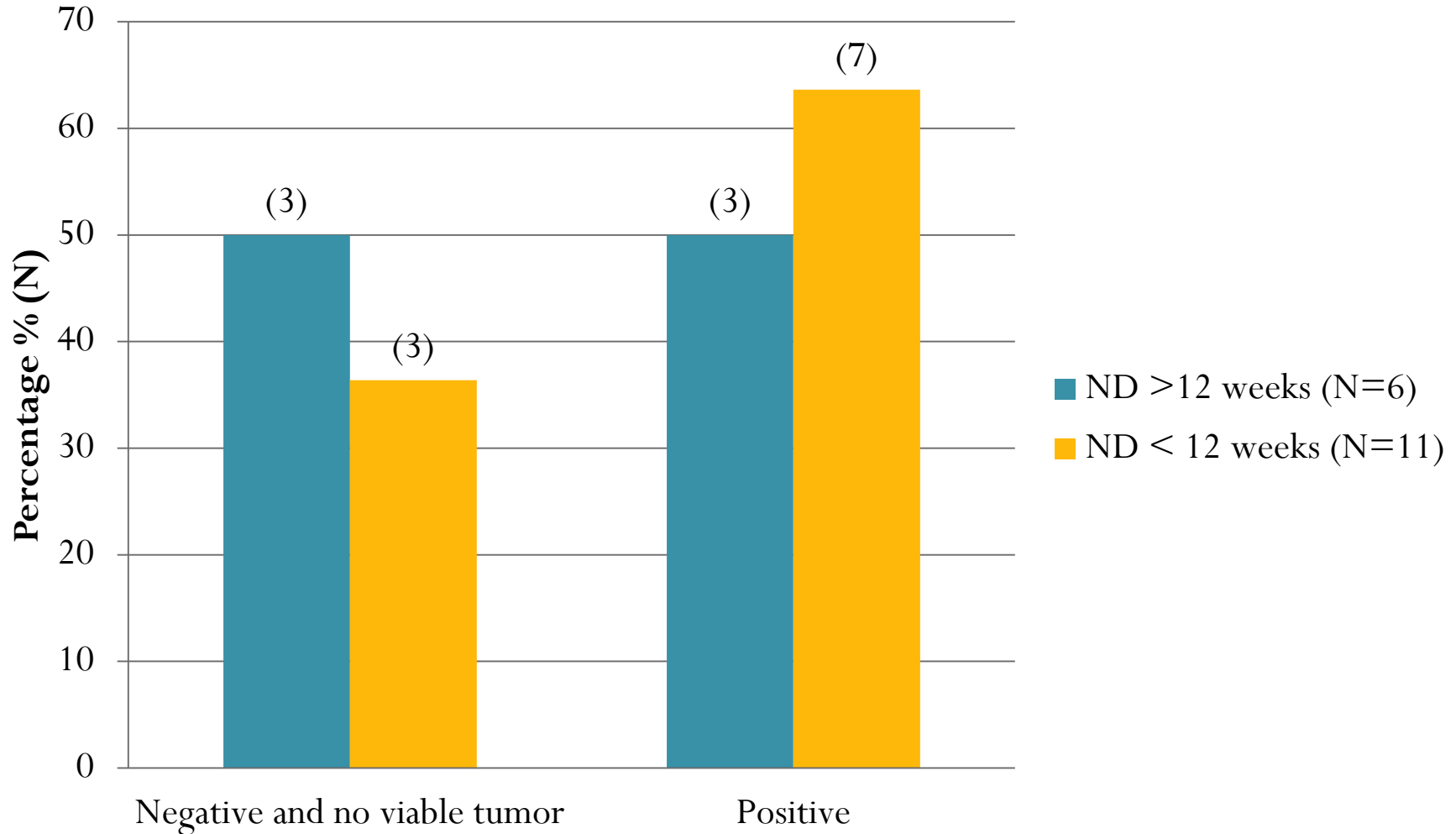
Patients pathological findings following a complete or partial response post chemoradiation



Pathological findings in specimens of patients with a complete response to chemoXRT (N=103)



Pathological findings in patients with a partial response to primary chemoXRT (N=17)



Outcomes following complete versus partial response

	Complete Response N=103 (%)	Partial Response N=17 (%)
Local Recurrence	4 (3.9)	5 (29.4)
Regional Recurrence	4 (3.9)	2 (11.8)
Second Primary	12 (11.7)	0 (0)
Distant metastases	12 (11.7)	5 (29.4)

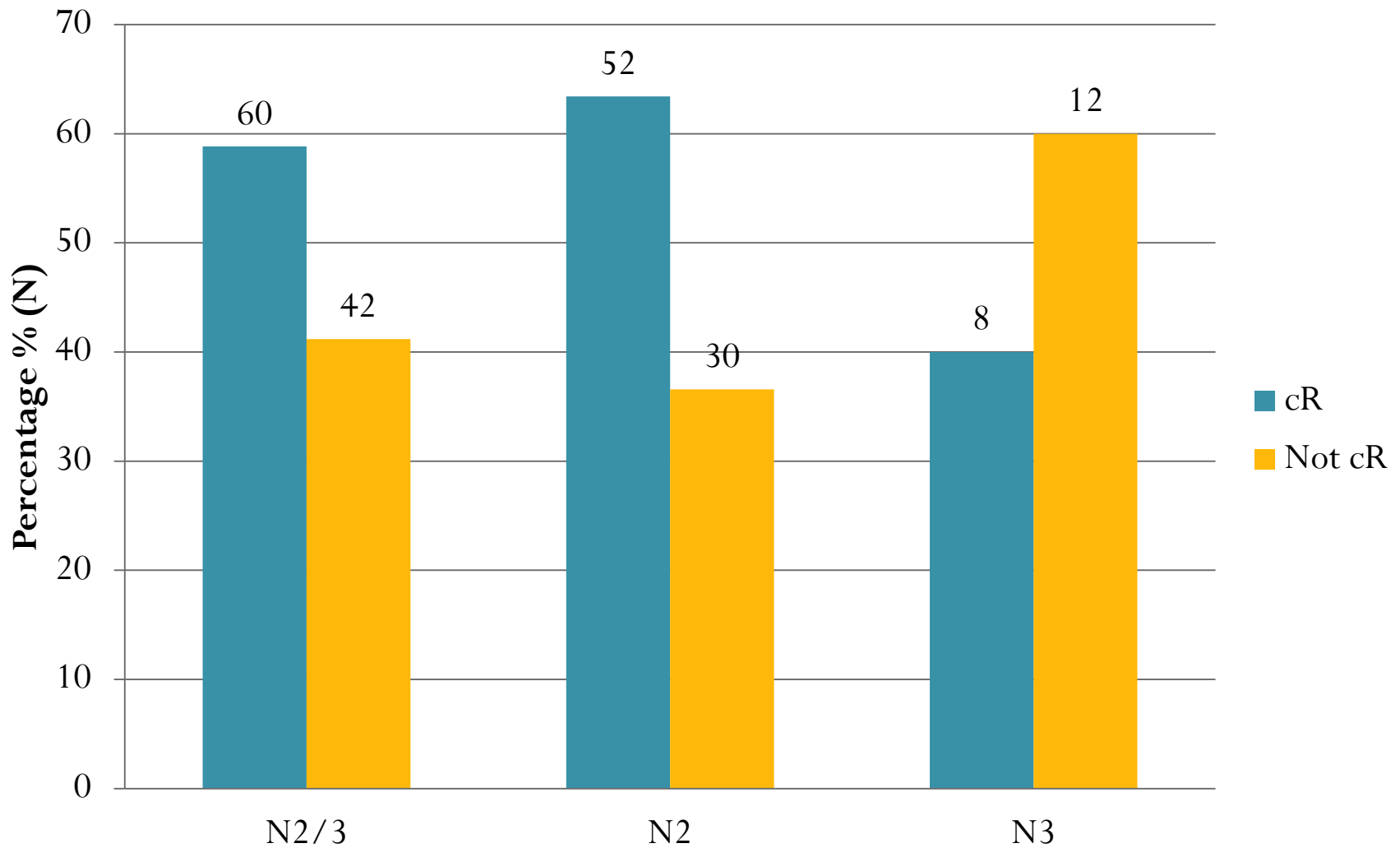
Planned neck dissection

- Is there a need for planned neck dissection in \geq N2 disease?

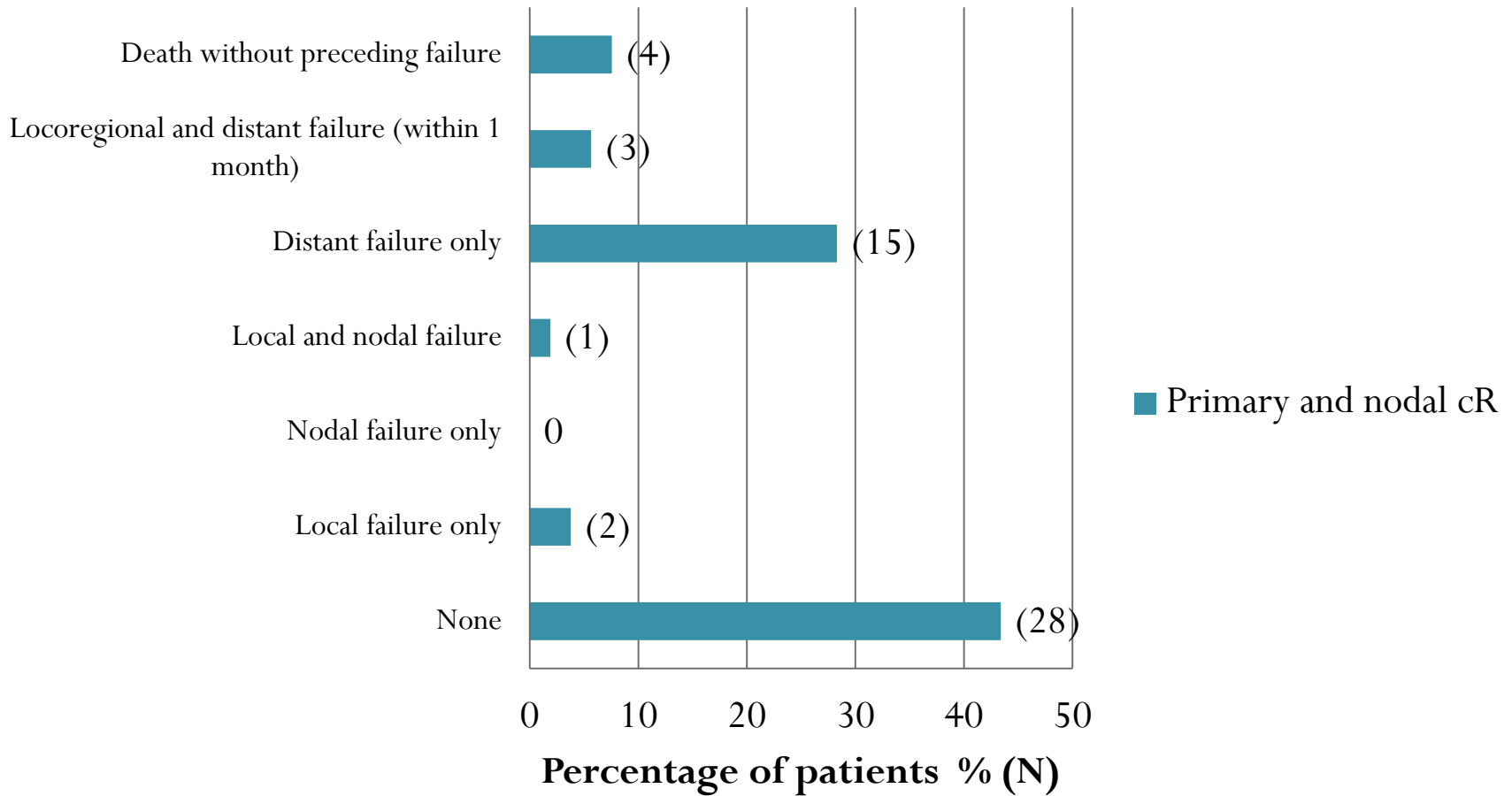
TROG 98.02 study

Aim	Radiation regimen	Concurrent chemotherapy	Monitoring
<ul style="list-style-type: none">• Prospective clinical trial• Identify incidence of isolated neck failure in patients with cR and \geq N2 disease 12 weeks post treatment	<ul style="list-style-type: none">• Radiation 7000cGy in 35 fractions over 7 weeks• Initial 5000 cGy encompassed gross clinical disease and suspected sites 7000cGy to macroscopic disease	<ul style="list-style-type: none">• Cisplatin (75mg/m²) and Tirazepine (290 mg/m²) or• Cisplatin (50mg/m²) and 5FU (360mg/m²)	<ul style="list-style-type: none">• Clinical and radiological assessment (CT) of treatment response at 12 weeks and 26 weeks post treatment

Response at 12 weeks by nodal classification (N=102)

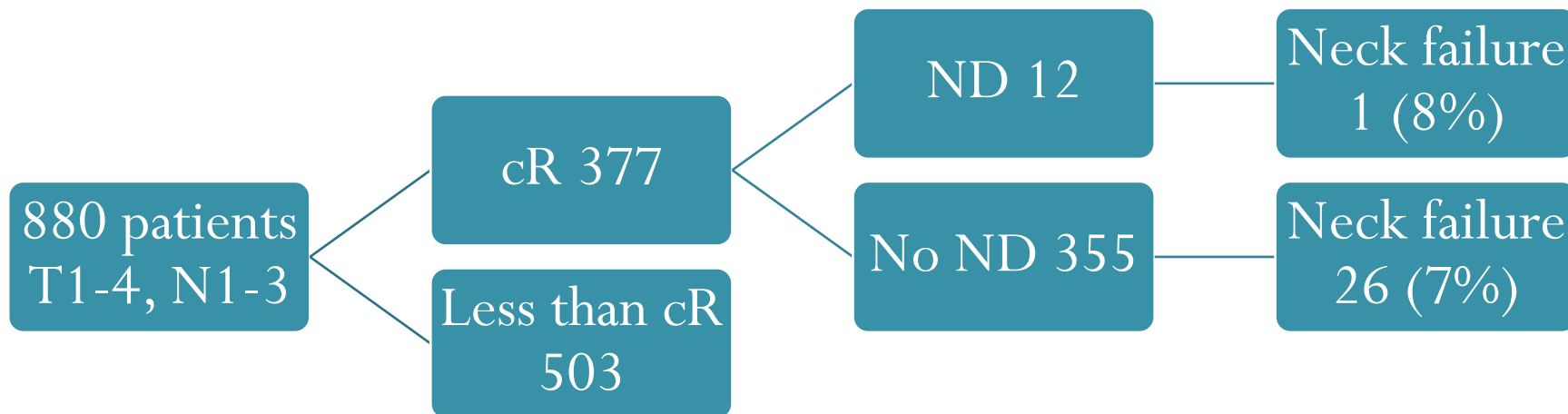


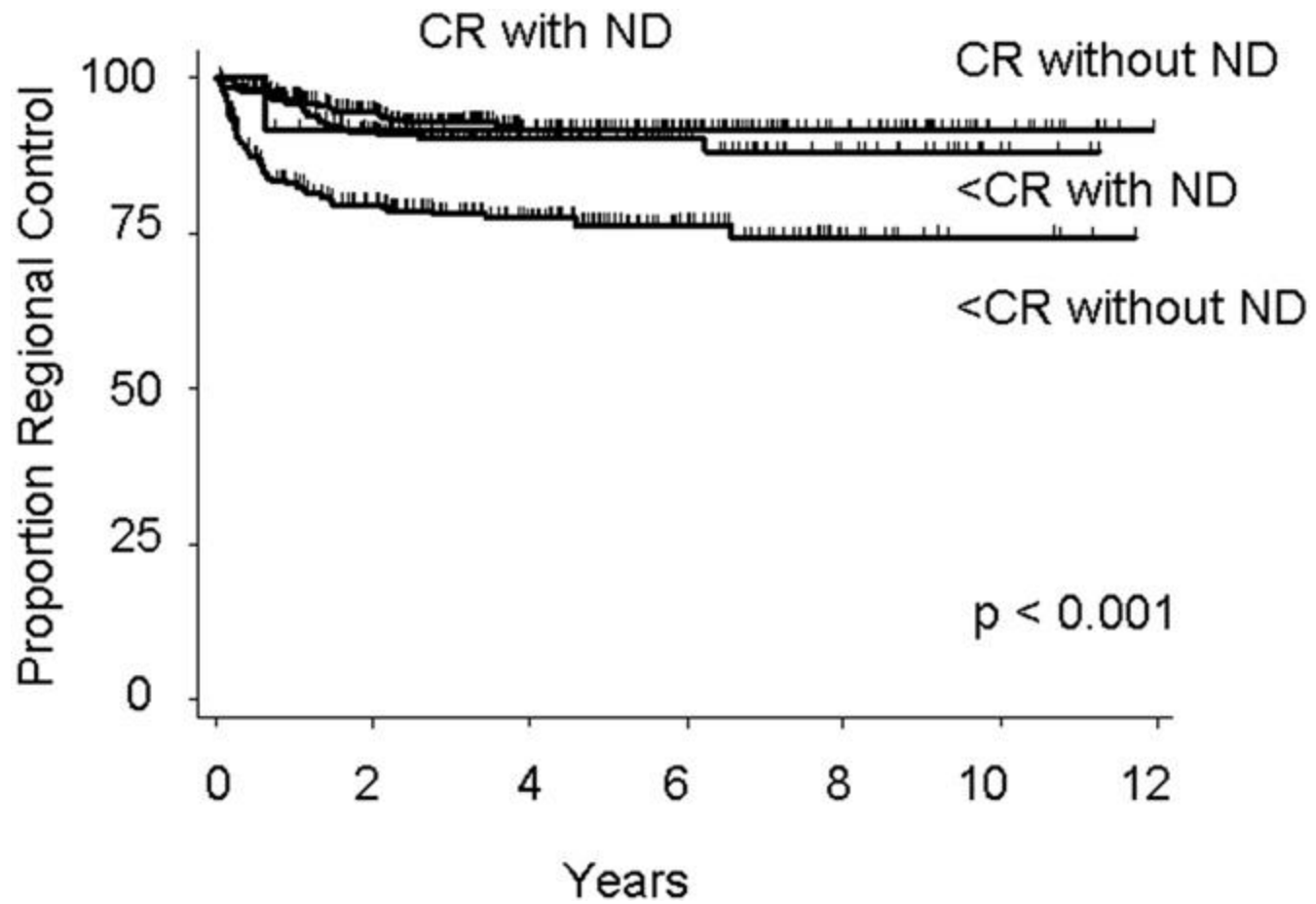
Patterns of failure in patients with \geq N2 disease with primary and Nodal cR (N=53)

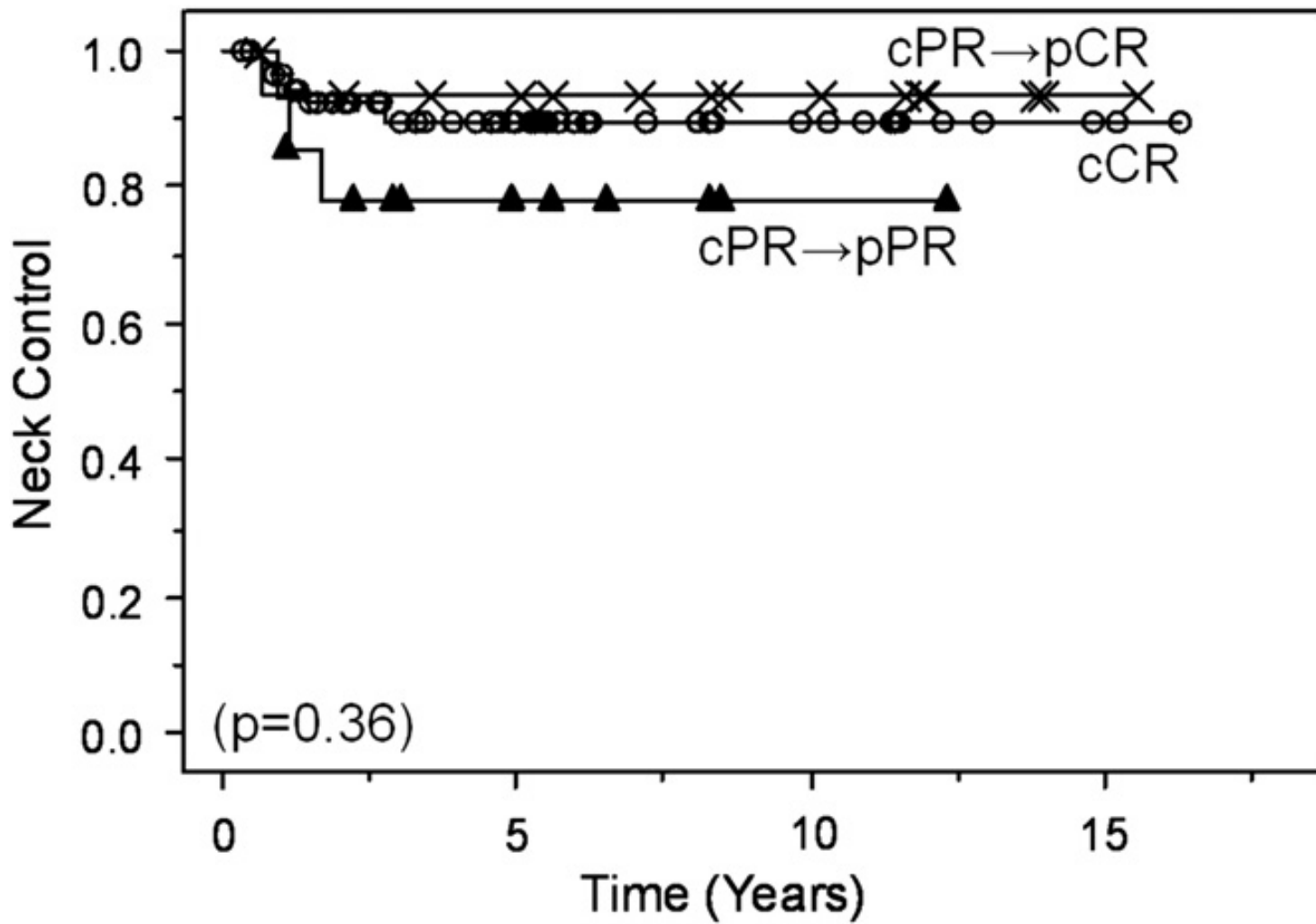


Retrospective Cohort Study MD Anderson

Aim	Radiation Regimen	Concurrent chemotherapy	Monitoring
<ul style="list-style-type: none">• Assess the need for planned ND following cR after radiation• Evaluate benefit of neck dissection in less than cR	<ul style="list-style-type: none">• Median dose to primary and nodes 7000cGy• Conventional or altered (twice daily or concomitant boost) fractionation• Dose was not limited in view of planned ND	<ul style="list-style-type: none">• Regimen not documented	<ul style="list-style-type: none">• Physical examination• Contrast-enhanced CT 4- 8 weeks after therapy







Planned Neck dissection

- Low rate of isolated neck failure
- Most failures either distant or primary site not neck
- With adequate irradiation of the neck if there is complete response in neck then there is no need for planned neck dissection in $\geq N2$ disease.

Timing of ND

- Concerns regarding
 - Swallowing impairment
 - Prolonged feeding tube need
 - Shoulder dysfunction
 - Impaired wound healing
 - Radiation related fibrosis

Timing of ND

Complication Class	ND < 12 weeks N=67 (%)	ND > 12 weeks N=38 (%)
At least 1 complication	24 (35.8)	5 (15.8)
Multiple complications	6 (9.0)	3 (7.9)
At least 1 wound	16 (23.9)	4 (10.5)

- No significant difference in overall survival or progression-free survival in ND < or > 12 weeks

Timing of ND

- Not worse if done > 12 weeks
- Important particularly with current disease monitoring, with imaging at ~ 12 weeks

Assessing response to treatment and need for Planned ND

- Clinical examination
- Ultrasound
- CT
- MRI
- PET/CT

PET/CT

Aim

- Retrospective analysis
- Assess role of PET/CT in predicting early treatment response at primary site and neck after Chemo XRT

Radiation Regimen

- Custom blocking and compensation or IMRT to primary site and neck 7000cGy

Chemotherapy regimen

- Intrarterial cisplatin (150 mg/m²)

Imaging

- PET/CT 6 weeks following completion of chemotherapy

PET/CT neck in Pretreatment positive necks

	Positive Neck	Negative Neck
PET/CT Positive	3	0
PET/CT Negative	1	17

- N = 21
- Sensitivity 75%
- Specificity 94%
- PPV 75%
- NPV 94%

PET/CT

Aim

- Retrospective review of the utility of PET/CT in patients with \geq N2 disease with cR prior to planned post treatment neck dissection

Radiation

- Mean radiation dose 7042 cGy

Chemotherapy

- Concurrent cisplatin or,
- Cisplatin and fluorouracil

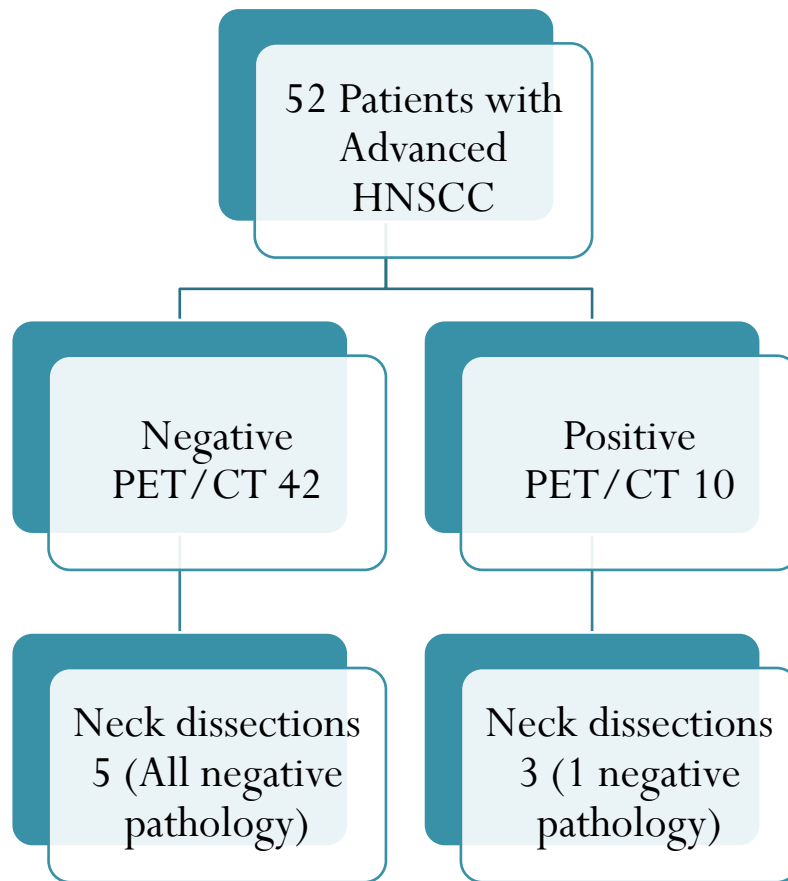
PET/CT

- 8-11 weeks after chemoXRT
- MRND at 11-12 weeks
- Sensitivity 60%
- Specificity 36%
- PPV 30%
- NPV 67%

PET/CT

Aim	Radiation	Chemotherapy	PET/CT
<ul style="list-style-type: none">Retrospective review of PET/CT imaging surveillance of post chemoXRT advanced HNSCC	<ul style="list-style-type: none">IMRT mean 6970 cGy to neck	<ul style="list-style-type: none">Unknown regimen	<ul style="list-style-type: none">Median 11.8 weeks post treatment (range 3.7 - 29.4)

PET/CT



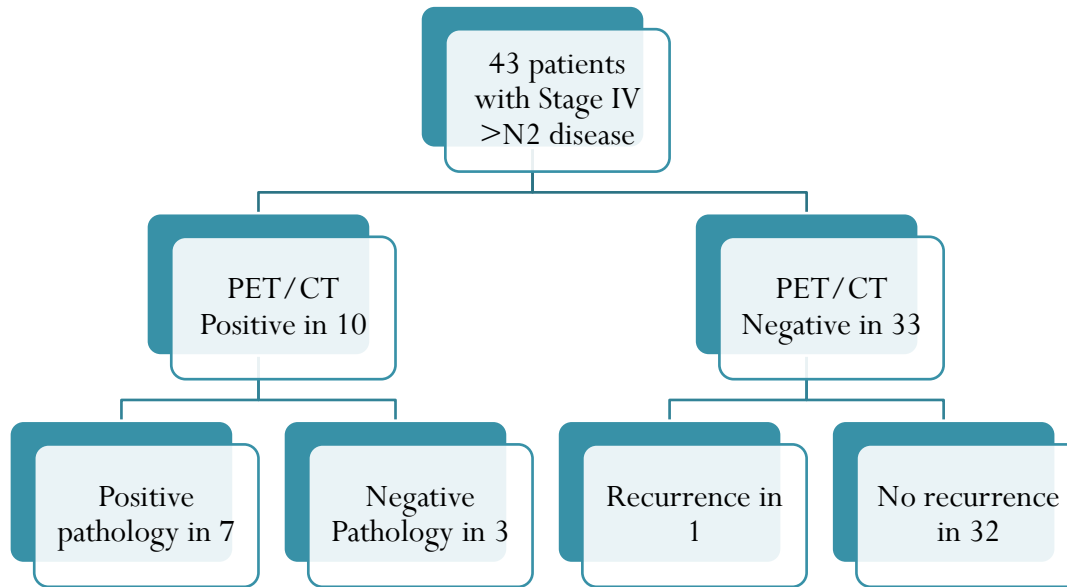
- Sensitivity 100%
- Specificity 87.5%
- PPV 40%
- NPV 100%

- No significant difference if PET obtained before or after 8 weeks

PET/CT

Aim	Radiation	Chemotherapy regimen	PET/CT
<ul style="list-style-type: none">• Observational study to determine PET/CT use in deferring planned neck dissection for patients with advanced HNSCC	<ul style="list-style-type: none">• Mean radiation dose 6410 cGy	<ul style="list-style-type: none">• Taxane or,• Platinum agent or,• Both	<ul style="list-style-type: none">• Obtained every 3-4 months

PET/CT



- Sensitivity 88%
- Specificity 91%
- PPV 70%
- NPV 97%

- In cohort 75% spared ND

PET/CT

- PPV is variable possibly related to timing of PET/CT
- Has a high NPV

PET/CT

Aim

- Prospective Study in omitting ND in all PET-negative nodes after definitive chemoXRT regardless of the presence or size of residual nodal abnormalities on contrast CT

Radiation

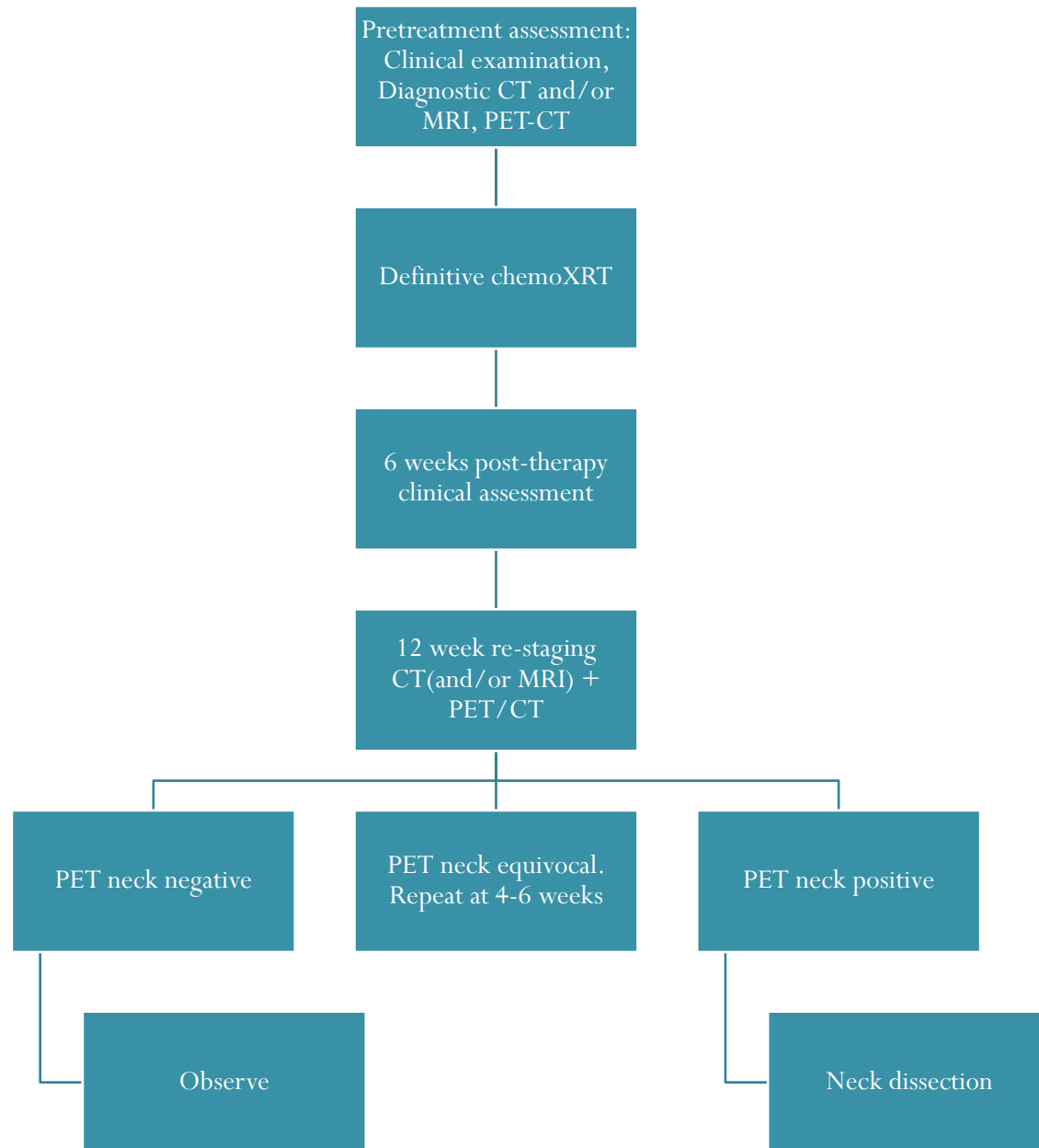
- Concomitant boost or fractionated RT
- 5000 cGy to elective sites
- 7000 cGy to known sites of disease

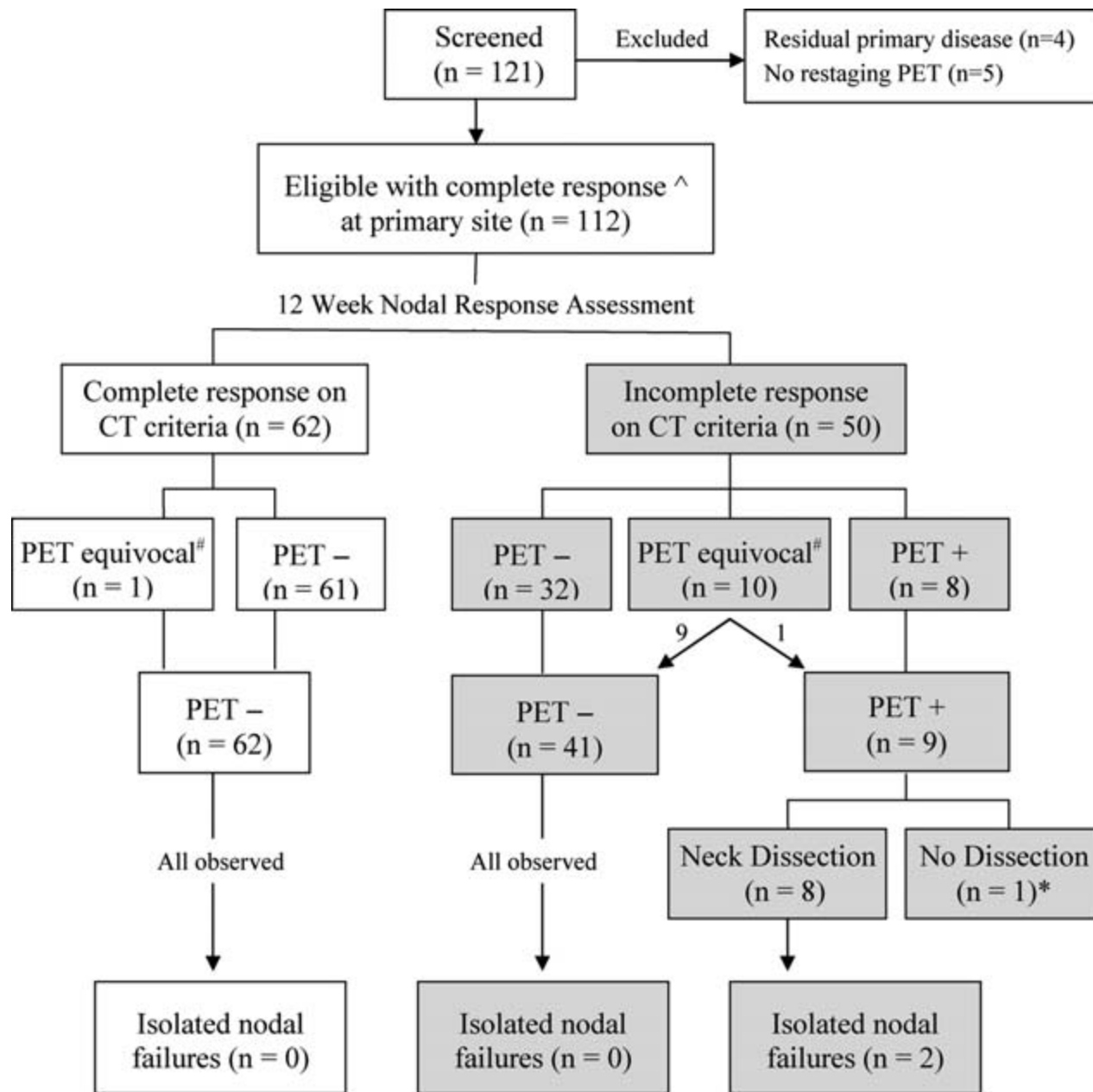
Chemotherapy

- Concurrent Cisplatin (100 mg/m²)

PET/CT

- PET within 3 weeks of commencing RT and 12 weeks post therapy.
- Diagnostic CT contemporaneously





PET/CT

	PET Alone (95% CI)	CT Alone (95% CI)
PPV	77.8 (40.0 – 97.2)	14.0 (5.8-26.7)
NPV	98.1 (93.2-99.8)	96.8 (88.8-99.6)

- Similar values in p16 positive group.

Response outcome in N2 patients (N=82)

	Pathology positive	Pathology negative
PET positive	3	2
PET negative	1	78

- PPV 60%
- NPV 98.7%

Response outcome in N3 patients (N=14)

	Positive Pathology	Negative Pathology
PET positive	2	0
PET negative	0	12

- PPV 100%
- NPV 100%

PET/CT

- Optimal timing for PET/CT inconclusive but generally around 12 weeks
- Cost effectiveness remains to be evaluated compared to ND
- No current SUV cutoff used that conclusively improves monitoring

Conclusions

- Planned neck dissection following complete response to primary chemoXRT has no significant added benefit in the adequately irradiated neck for neck control
- Response monitored clinically and with PET/CT
- Delaying ND after 12 weeks has no significant consequence
- Need further to evaluate in HPV population