Safety and clinical implications of concurrent biopsy of neuroendocrine liver metastases at the time of liver-directed therapy

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Background

- Ki-67 and histopathological tumor grade of NELM inform patient prognosis
- Both are important in guiding clinical management
- Temporal changes in Ki-67may exist. How often a change in grade is observed and how frequently therapy changes as a consequence remain poorly understood
- Liver-directed therapy is often performed at times of tumor progression. It may present a safe opportunity to obtain percutaneous biopsies at the same time, which can be useful for re-grading, future treatment planning and patient prognosis.

Figure 1. OS of patients with >2% rise in Ki67/year

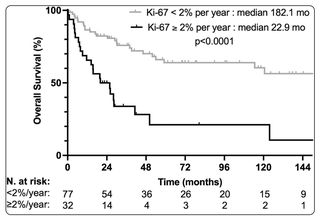

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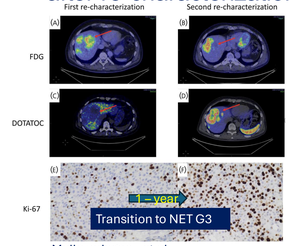
Figure 2. Change in grade after re-characterization



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Aim

1. To assess the safety profile of percutaneous core biopsies of NELM acquired during LDT
2. Evaluate Ki-67 and grade in these samples in comparison to priors to assess change over time
3. Determine whether data obtained from these biopsies influences therapy

Methods

- Patients with clinically diagnosed NETLMs were enrolled in a prospective cohort study for genetic, proteomic and metabolic characterisation of NETLMs at a single academic center from 2016-2024 (IRB#825782).
- 18G core biopsies were obtained using coaxial technique at the time of LDT.
- Study data, including biopsy complications, were collected prospectively using a Research Electronic Data Capture. Patient charts were reviewed in a retrospective fashion at the time of this study to gather additional clinical information.

Outcomes

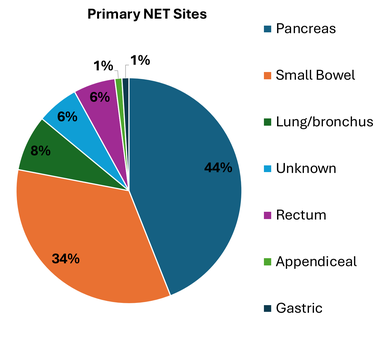
Primary Outcome
- Overall complication rates associated with obtaining core biopsies immediately before liver-directed therapy
- Major and minor complication rates using the Society of Interventional Radiology guidelines

Secondary Outcome
- Change in tumor grade
- Change in management based on grade
- Association between AEs and patient demographics

Statistical Analyses
- Pearson's chi-square, t-test and Wilcoxin rank sum
- Univariate logistic regression

Results

Patient Characteristics N=87	n	%
Age, mean (SD)	77(11)	
Sex, male	40	52
ECOG performance 0-1	72	94
Extrahepatic Mets	34	44
Years from primary DX, median (range)	1.7 (0.7-3.5)	
Prior therapy		
SSA	71	92
Liver Directed Therapy	28	36
Cytotoxic Chemotherapy	28	36
PPRT	12	16
Everolimus/Sirolimus	10	13



Safety of percutaneous biopsies of NELM acquired during LDT (n = 87)

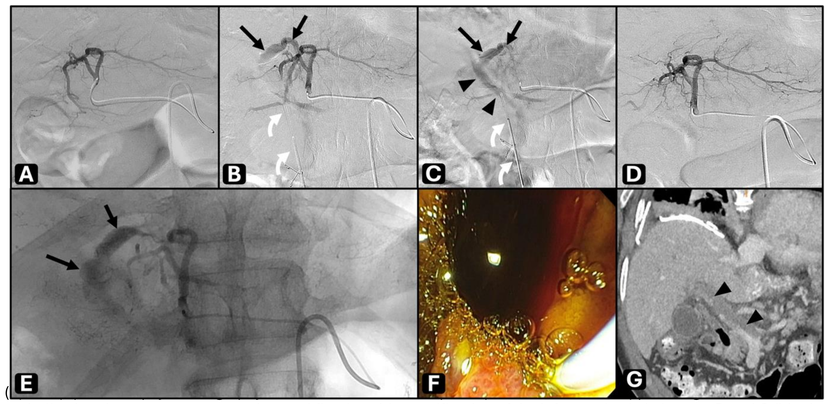
Complications	AE Severity	Intervention performed
1. Arterioportal fistula	Mild	-
2. Portal vein thrombosis with hepatic necrosis	Mild	-
3. Subcapsular hematoma	Mild	-
4. Perihepatic hemorrhage	Mild ⚠	Bland emobilization
5. Arteriovenous fistula	Mild ⚠	Gelfoam embolization
6. Arterioportal fistula with subsequent portal vein thrombosis	Major ⚠	ERCP + Anticoagulation
7. Subcapsular/perihepatic hematoma with hemoperitoneum	Major ⚠	Gelfoam embolization

⚠ *Complications requiring intervention*

Minor AEs: *Requiring no therapy/receiving nominal therapy (embo during LDT)*

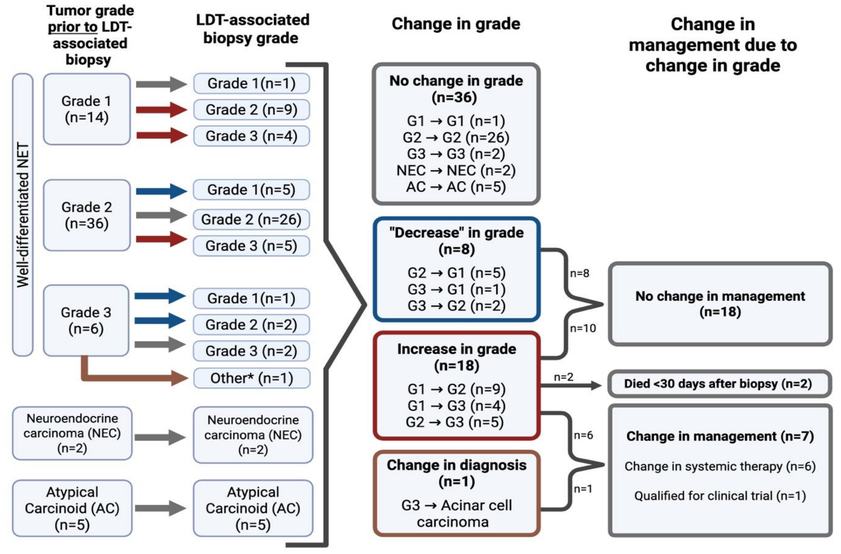
Major AEs: *Requiring additional intervention*

- Overall AE associated with biopsy: 8% (7/87)
- Major complications: 2% (2/87)
- Minor complications: 6% (5/87)
- Bleeding complications: 5% (4/87)



embolization demonstrates an arterioportal fistula, with opacification of the left portal vein in images B and C (black arrows) and main portal vein in image C (black arrowheads). (D) After gelfoam tract embolization, the arterioportal fistula is no longer seen. (E) Despite apparent resolution on arteriography, chemoembolic material is seen staining the left portal with extension into the main portal vein after chemoembolization (black arrows). (F) Hemobilia, likely a result of arteriobiliary fistula, was identified on ERCP 11 days later, which resulted in biliary obstruction and cholangitis. (G) Serial imaging demonstrated left portal vein thrombosis which progressed to main portal vein thrombosis, as demonstrated by the black arrowheads.

Figure 5. Changes in Grade and Subsequent Therapy (n = 63)



- 27/63 (43%) patients' tumor grade changed
- 7/18 (39%) patients' grade progression resulted in a change of management
- NNT = 9

- **There was no significant association between AEs and clinical characteristics (biopsy location, number of cores, etc). AEs were assessed by univariate analyses. Significance was set at p<0.05.**

Conclusion

- Ki-67 may change as the disease progresses
- Repeat biopsy at the time of LDT may provide valuable insights into grade progression and subsequent management
- **Percutaneous biopsy of NET liver metastases immediately prior to LDT showed an acceptable adverse event rate, comparable to standalone biopsy, although with a unique complication profile**

Future Outlook

- Evaluate hPFS and OS in those who demonstrated no change in grade versus those that did – determine how much grade change affected prognosis
- Larger studies to validate potential predictors of biopsy –related complications and better characterize safety profile
- Better define the timepoint for re-assessment with serial biopsy

References

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