Benefit for Liver QOL from Single Radiation Treatment in End-stage Liver Cancer/Liver Metastases: CCTG HE.1 Phase III RCT (NCT02511522)

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Introduction

- Patients (pts) with advanced liver malignancy (primary or metastatic) often have pain
- Medical management can be challenging and pain incompletely relieved
- Those at end of life without systemic therapy options may benefit from radiotherapy (RT)[1]
- Pain reduction is the primary goal but QOL is an important secondary endpoint

Methods

- A multicentre phase III RCT in HCC/LM pts with moderate-severe (BPI >4) liver pain
- Pts randomized 1:1 to best supportive care (BSC) plus RT (8Gy/1) versus BSC alone
- All pts on RT arm were pretreated with dexamethasone 4mg/granisetron 1mg
- Median follow-up 3.2 months
- Eligibility: End-stage disease unsuitable for other therapies
  - o >4 weeks since chemotherapy or TACE
  - o >2 weeks since targeted or immunotherapy
  - o No planned systemic therapy
- Endpoint: Functional Assessment of Cancer Therapy -Hepatobiliary (FACT-Hep) hepatobiliary subscale (HBS)
  - o Clinically important benefit was change score ≥5 at 1 month

Figure 1: Study Schema

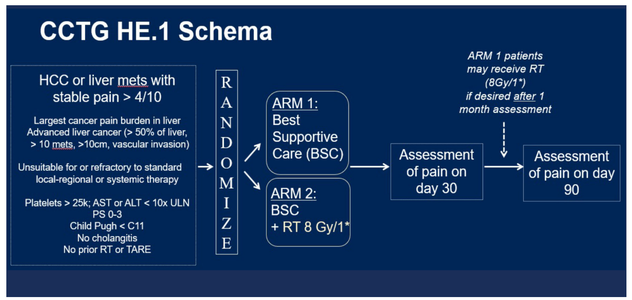
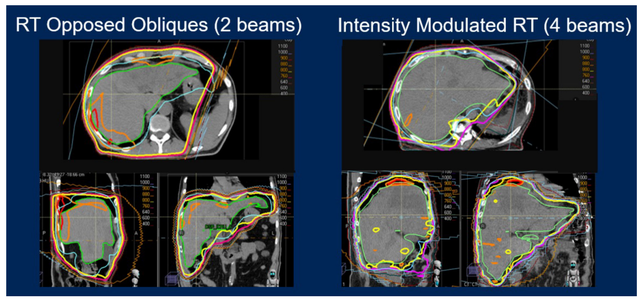


Figure 2: Sample (Simple) Radiotherapy Plans



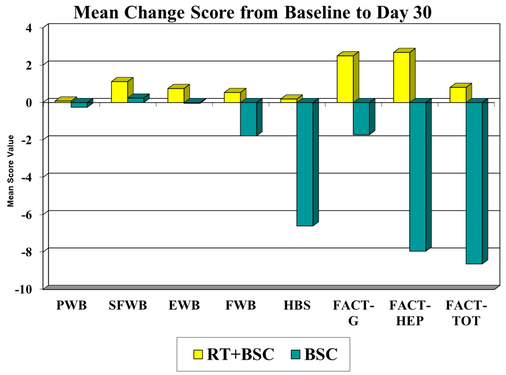
Results

- o 66 pts randomized
- o poor ECOG PS: 2/3 in 59%
- o Hepatocellular carcinoma (HCC)- 23 pts
- o Liver metastases (LM) - 48: colorectal (10), breast (8) pancreas (4), other (26)
- o Eleven BSC patients crossed over to RT after 30 days
- o The primary endpoint showed improved pain (BPI at 1 month post-treatment[2])
- o Overall survival (3 months) was 51% RT/BCS vs. 33% BSC, p=0.07
- o QOL completion was: baseline 100%, 1 month 86%
- o Mean change score at 1 month showed a trend favouring RT/BSC
- o 0.19 (sd 9.43) RT/BSC vs -6.6 (sd 12.31) BSC alone (p=0.07)
- o No statistically significant difference in other FACT-Hep subscales

Table 1: QOL response assessment in 42 analyzable patients

QOL response assessment – FACT-Hep HBS	RT+BSC N (%)	BSC N (%)	CMH P-value (*)
Patients with QOL at baseline and day 30	24	18	
Clinically significant improvement (≥5 point change)	9 (37.5)	4 (22.2)	0.29
Clinically significant worsening (≥-5 point change)	8 (33.3)	11 (61.1)	0.08
Stable (between -5 point and 5 point change)	7 (29.2)	3 (16.7)	0.36

Figure 2: Mean change score from baseline to 1 month by arm for HBS, FACT-Hep and subscales



Opioid Use:

- o Most patients (26 RT/BSC, 29 BSC) required opioids at baseline
- o BSC/RT showed a trend to reduced requirements (-6.25 morphine mg-eq/day)
- o BSC alone showed increased requirements (+34 mg-eq/day)

Table 2: Percentage of pts who stopped or reduced opioids from baseline to 1 month

Patients alive and evaluable at 30 days who were taking opioids at baseline	RT+BSC N (%) N=19	BSC N (%) N=16	CMH P-value (1)
Patients stopped opioids or with 25% Reduction in Opioid Use(2)	10 (52.6)	5 (31.3)	0.20

(1) Stratified Cochran-Mantel-Haenszel test adjusting for the stratification factor (HCC versus liver metastases)

(2) 25% Reduction in opioid use from baseline to day 30 (employing daily morphine equivalence scale).

Conclusions

- Single fraction RT (8 Gy) resulted in a trend of clinically-important magnitude for between-groups difference of liver-specific QOL change from baseline to 30 days in end-stage patients with moderate-severe liver pain
- Simple, whole or near-whole liver single fraction RT can be delivered safely in any radiation oncology centre with minimal burden to pts
- Given statistically and clinically significant reduction in pain and trend to improved survival, this intervention SHOULD BECOME STANDARD OF CARE

References

1. Soliman H, Ringash J, Jiang H, Singh K, Kim J, Dinniwell R, Brade A, Wong R, Brierley J, Cummings B, Zimmerman C, Dawson LA. Phase II Trial of Palliative Radiotherapy for Hepatocellular Carcinoma and Liver Metastases. J Clin Oncol. 2013 Nov 1;31(31):3980-3986
2. Dawson LA, Fairchild A, Dennis K, et al. CCTG HE.1 Phase III Study of Palliative Radiotherapy for Symptomatic Hepatocellular Carcinoma and Liver Metastases. ASCO-GI, Jan.20, 2023

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