Efficacy of Yttrium-90 or Drug-Eluting Bead (DEB) Therapy for Patients with Unresectable Colorectal Liver Metastasis After Prior Avastin Treatment.

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Introduction

- Colorectal cancer is the 2nd most common cause of cancer related deaths in the US
- Surgical resection of the liver is the only curative treatment for patients.
- Most Patients (70%) are not eligible for resection at time of diagnosis because of disease volume
- DEB or Y-90 therapy is a viable treatment option for unresectable CRLM to reduce tumor burden
- Bevacizumab (Avastin) works by selectively binding to Vascular endothelial growth factor A (VEGF), which inhibits the binding of VEGF to the cell surface
  - The inhibition leads to a reduction in angiogenesis of tumor blood vessels thus limiting blood supply to the tumor

Purpose of Pilot Study

- The aim of this study is to determine the tumor response rate of patients receiving DEB or Y-90 as second-line or bridge chemotherapy after prior first-line treatment with Avastin.
- It was hypothesized that prior Avastin would make a difference in the hepatic arterial therapy (HAT) response
- Because Avastin decreases angiogenesis, DEB or Y-90 will have fewer blood vessels to implant in, giving a different amount of radiation

Methods

- A University of Louisville institutional review board (IRB)-approved prospective study evaluated patients from 2003 to present, in which 296 patients were reviewed to compare different response rates.
- Informed consent was obtained from the subjects prior to evaluation and screening.
- Inclusion criteria include the following:
  1. Patient diagnosed with colorectal liver metastasis with liver dominant metastasis
  2. Patient has received only one prior line of chemotherapy before beginning HAT
  3. Patient completed first-line chemotherapy.
- The study focuses on the differing tumor responses of yttrium-90 or drug-eluting beads irinotecan after prior first-line systematic chemotherapy of Avastin as compared to other chemotherapies w/o Avastin.
- Tumor Response was measured using RECIST 1.1 criteria

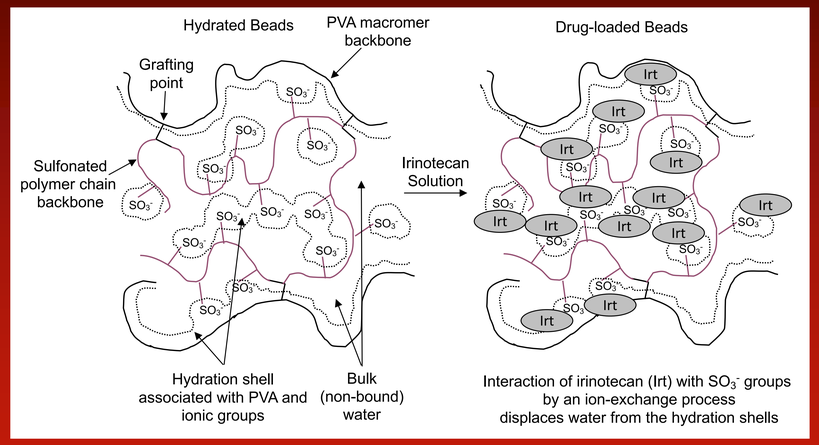

Figure 1. Drug-eluting bead loading Irinotecan mechanism

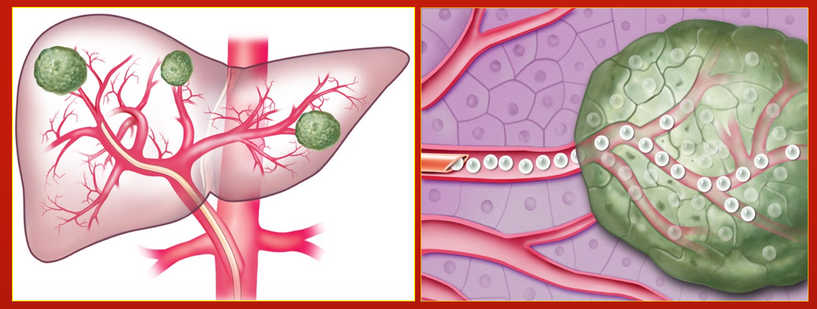

Figure 2. Y-90 Sphere Administration
Y-90 Sphere size is small enough to gain entry into nodules but too large to pass through the end capillary bed into the venous circulation

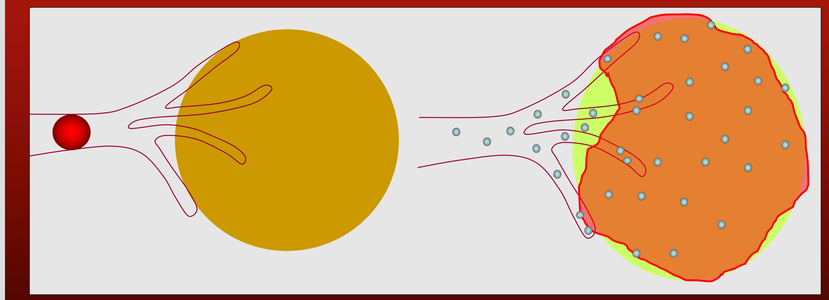

Figure 3. Chemoembolization (Left) compared to Radioembolization (Right)

Acknowledgments

Research was supported by the University of Louisville Cancer Education Program and the NIH/NCI (R25-CA134283) grant.

Results

Table 1. Patient Demographics

Characteristic	Prior Avastin (n=25)	No Avastin (n=27)
Median age, y (range)	61 (35-78)	60 (42-90)
Sex: Male/female, No.	16/9	14/13
Race: African American/White /Hispanic, No.	3,19,1	3,15,0 (some unknown)
CEA prior to treatment, median (range)	61.1 (0.31-5370)	76.9 (1.96-4760)
Bilobar disease, No. (%)	21 (84%)	10 (37%)
No. of target lesions	2 (1-5)	2 (1-4)
Prior Treatments, *No. Treatments Given*	**Treatments Given, No.**	**Treatments Given, No.**
FOLFOX	24	16
FOLFIRI	13	3
Xeloda	2	5
Vectibix	1	3
Keytruda	1	1
Erbitux (Cetuximab)	1	1
XRT 5-fluorouracil	1	NA
Prior Treatments, *No. Cycles*	**Median Cycles, No. (Range)**	**Median Cycles, No. (Range)**
FOLFOX	12 (1-14)	12 (3-12)
FOLFIRI	12 (3-23)	10.5 (6-12)
Avastin	10 (2-13)	NA
Xeloda	6	6
Vectibix	NA	8 (4-12)
Keytruda	5	4
Erbitux (Cetuximab)	23	1
XRT 5-fluorouracil	6	NA
Time to HAT from last chemotherapy *Average, Median No. weeks (range)*	27.9, 11.1 (3 – 153)	12.5, 0 (6.9 - 64.1)

Table 2. All Adverse Events in Patient Cohort

Adverse Events	Avastin Patients	Non-Avastin Patients
All Adverse Events, No.	10	8
Aches	1	0
Nausea	2	4
Vomiting	1	1
Fatigue	4	2
Hypertension	1	0
Groin Bleeding	1	0
Constipation	0	1

Table 3. RECIST Tumor Response Data for Patient Cohort

Prior treatments	Prior Avastin (25 Patients, 45 Treatments)	No Avastin (27 Patients, 45 Treatments)
RECIST Response, No. (%)		
Complete Response	0 (0%)	2 (4%)
Partial Response	5 (11%)	3 (7%)
Stable Disease	27 (60%)	17 (38%)
Progression of Disease	8 (18%)	7 (16%)
Expired From Disease	15 (60%)	10 (37%)
CEA Post treatment, Median (Range)	55.1 (1.12-3640)	42.2 (2.92-1010)

- A total of 52 patients were examined for the study.
- Most patients presented with Stage IV disease at onset of HAI treatment.
- Patients received prior chemotherapy with most receiving FOLFOX for a median of 12 cycles.
- Majority of patients had stable disease for both groups.
- Adverse events were kept to a minimum and low grade.
- Initial statistics show no significant difference in response rates/ lesion size for prior Avastin on Y-90 or DEB treatments.
- More stable disease for prior Avastin patients can be attributed to decreased angiogenesis from Avastin.

Conclusions

- Contrary to previous study, this study demonstrated that prior Avastin has only a small effect on the tumor response rate, and ultimately the resectability rate of target lesions using DEB.
- Y-90 and DEB offer an effective and safe method to target lesions to try and increase resectability, but prior Avastin shows no statistically significant difference in lesion size change.