Improving the care of hepatocellular cancer patients

REPORT FROM THE 15TH ANNUAL WESTERN CANADIAN GASTROINTESTINAL CANCER CONSENSUS CONFERENCE, WINNIPEG, MANITOBA, SEPTEMBER 5-7, 2013

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 TERMS OF REFERENCE

Purpose
This is a consensus opinion of oncologists and allied health professionals from across Western Canada intended to define best care practices and improve outcomes for patients with hepatocellular cancer (HCC).

Participants
Medical, radiation and surgical oncologists and allied health professionals involved in the care of patients with HCC, including leaders from the United States and across Canada.

Target audience
Healthcare professionals involved in the care of HCC patients.

Basis of recommendations
The recommendations provided are on the basis of best available evidence. A brief summary of each consensus statement is presented along with the discussion that led to the consensus statement.

The meeting’s goal is to improve the quality and uniformity of gastrointestinal cancer care in the Western provinces, and is attended by provincial leaders in medical, radiation and surgical oncology. The topic of this year’s conference was HCC. The conference had presentations by leaders in HCC care across North America, and consensus statements were developed after discussion of the information presented.

Conference sponsors
The conference was supported by sponsors who provided an unrestricted educational grant: Amgen, Roche, Sanofi, Bayer, Bristol-Myers Squibb and Genomic Health.
CONSENSUS

GENERAL STATEMENT

1. Care of the HCC patient should be in a multidisciplinary team consisting of a hepatologist, hepatobiliary surgeon, medical oncologist, diagnostic and interventional radiologist, radiation oncologist, pathologist, palliative care specialist, nurse, pharmacist and other supportive oncology professionals.

Summary of discussion
A common theme through many of the talks was the complexity and variety of treatment options for HCC. Decision-making is often complex and involves many specialties, including some that are unique to this disease site (e.g. hepatology and interventional radiology). There was broad consensus that patients with HCC should be treated in a multidisciplinary fashion and, given the rarity of the disease, by a team with solid experience in HCC. This was a general theme that recurred throughout the meeting.

SYSTEMIC THERAPY

2. Sorafenib is the recommended treatment for Eastern Cooperative Oncology Group (ECOG) 0–2 patients with Child-Pugh A liver function who are not candidates for local therapy (as per the Barcelona Clinic Liver Clinic staging classification [BCLC]). Consideration should be given to enrollment in clinical trials if available.

Summary of discussion
Dr. Jennifer Knox from Princess Margaret Hospital provided an update on current and future systemic therapies for HCC. Her talk highlighted the results of the SHARP trial of sorafenib in Child-Pugh A patients that showed an increase in median overall survival (OS) of 10.7 versus 7.9 months. A second Asian study and registry dataset confirmed these findings. Dr. Knox highlighted the need to manage side effects while on treatment, and gave an excellent overview of emerging clinical trials of novel agents, new drug combinations and expanded treatment indications.

The group was unanimous in supporting the use of sorafenib as standard of care in Child-Pugh A patients who are not candidates for local therapies. With several clinical trials ongoing, there was enthusiasm for encouraging enrollment in clinical trials wherever resources permit.

3. Outside of a clinical trial, Child-Pugh B7 or higher patients should not be routinely treated with sorafenib, due to lack of evidence.

Summary of discussion
Dr. Janine Davies from the BC Cancer Agency, Kelowna, outlined the pros and cons of sorafenib in Child-Pugh B patients. Her information was supplemented by Dr. Knox’s overview of systemic therapy. Dr. Davies highlighted that Child-Pugh B patients have shortened survival due to the advanced nature of their liver function impairment. She then reviewed several small phase 1 and 2 studies looking at outcomes in Child-Pugh B patients on sorafenib. Indeed, survival was meager and toxicities higher in this population. For example, a study by Abou-Alfa published in Gastrointestinal Research in 2010 found 38 patients with Child Pugh B liver function had a median OS of only 3.2 months with sorafenib treatment, and experienced high rates of grade 3–4 toxicity. Other small studies found similar results.

There was general consensus in the group that sorafenib should not be routinely offered to Child-Pugh B patients. There was active discussion as to whether B7 patients, or those with liver function approaching Child-Pugh A, should be treated differently. The majority of participants did not support sorafenib use in B7, with a vocal minority saying that in exceptional circumstances of excellent performance status, it may be appropriate with close monitoring.

RADIATION THERAPY

4. In patients who are not eligible for, or have progressed through, other local regional treatments, stereotactic body radiation therapy (SBRT) can be considered if there is adequate liver reserve and minimal or no extrahepatic disease. Cases should be reviewed in a multidisciplinary conference that includes a radiation oncologist with SBRT expertise. Enrollment in clinical trials is strongly encouraged (e.g.: RTOG 1112).

Summary of discussion
The group was pleased to hear from Dr. Laura Dawson, also from Princess Margaret Hospital, who is a renowned world expert on SBRT and its application to HCC. She outlined the practice of this technique in general and then proceeded to show results to date in HCC. She summarized case series showing a local response rate of 70% to 90% and 2-year OS of 43% to 82%. Dr. Dawson’s own case series of 102 patients showed an 87% one-year OS rate. She also introduced the RTOG 1112 study, on which she is the principal investigator. This international, multi-institution randomized controlled trial will likely be the definitive trial of this technique in HCC.

The group welcomed another treatment modality for this challenging disease. There was consensus that it is a valid option when provided in centres with the required expertise, and there were calls to increase access and expertise in the Western provinces. There was much enthusiasm about enrolling patients in the RTOG trial where resources and expertise exist.

INTERVENTIONAL RADIOTHERAPY

5. Various interventional radiology techniques are available, and decisions about their use are best made in a multidisciplinary setting.
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- When patients are not surgical candidates, radiofrequency ablation (RFA) may be considered for lesions less than 5 cm.
- Transarterial chemoembolization (TACE) should be available for patients who are not candidates for surgical resection/RFA, based on Level I evidence. Criteria include lack of portal vein thrombosis, ECOG 0–1, Child-Pugh B7 or lower, bilirubin <34 mmol/L, minimal extrahepatic disease and adequate organ function.
- Transarterial radioembolization (TARE) with Yttrium 90 can be considered as downstaging therapy for liver transplant or resection in patients with locoregional disease ECOG 0–1 with Child-Pugh B7 or lower liver function who have failed, or who are not candidates for, TACE. Portal vein thrombosis is not a contraindication for TARE.
- Enrollment in clinical trials, where available, is strongly encouraged.

Summary of discussion
The role of interventional radiology was presented by Dr. Richard Owen, interventional radiologist with the University of Alberta. The performance of RFA, TACE and TARE were explained to the group. Contraindications and complications were also discussed. The best evidence for radiologic procedures comes from TACE, which has been subjected to multiple randomized controlled trials. Phase 2 data on the utility of TARE are quite promising, but access is currently limited to a few centres.

The group supported aggressive use of these local strategies in appropriate patients. The key role of the interventional radiologist in this disease was emphasized and highlights the need to work in a multidisciplinary fashion. Further study in randomized controlled trials was encouraged to more precisely define the utility and effect size of these treatments.

ACCESS TO CARE

6. Given the subspecialized skill set needed, access should be limited to those facilities that are able to provide experienced multidisciplinary care. Embolization and ablation expertise should be available in every province, and is the expected standard care in any tertiary facility caring for HCC patients. Access to TARE and SBRT should be available, but the group recognized that patients may need to travel to centres of excellence to receive them.

Summary of discussion
There was much discussion around the disparity in access to treatment modalities across different provinces. A great deal of concern was expressed that some patients are almost certainly not receiving optimal care due to lack of access to a full multidisciplinary team with expertise in HCC. It was noted that even relatively basic techniques, such as RFA and TACE, are not available in all provinces. There was overwhelming consensus that access to care must be improved. It was felt that there is adequate expertise to recommend that RFA and TACE be available within the tertiary care centres of all Western provinces. Emerging techniques, such as TARE and SBRT, should also be available to all patients, but it would be reasonable for them to travel to centres of excellence to receive that care. Physicians treating these patients, hospital administrations and provincial governments need to support optimal care wherever the patient lives.

BRIDGING TO TRANSPLANT

7. Patients with early-stage HCC should be evaluated by a transplant team and waitlisted for transplant as per local transplant guidelines. RFA, TACE and other local therapies are accepted bridging techniques and should be employed within a structured transplant program.

Summary of discussion
An overview of criteria for transplant and strategies to bridge eligible patients to transplant was presented by Dr. Kelly Burak, director of the University of Calgary liver unit. He reported that OS from liver transplant for HCC is at least 70% in high volume centres. While Milan criteria were the first to be widely adopted for transplant, various centres are expanding on those criteria based on emerging evidence. Given the shortage of available organs for transplant, strategies are required to control disease and minimize patient dropout. Dr. Burak presented data showing the safety of this approach.

The group felt that it did not have the expertise to comment on the validity of the current transplant criteria in Canadian centres, but wholly supported the transplant teams in their own decision-making process. The group felt comfortable with and had experience in employing bridging strategies. Given the complexity of delivering this care, the need for a multidisciplinary approach and good communication was reiterated.

NEED TO BIOPSY

8. HCC can usually be diagnosed with a high degree of certainty using appropriate radiologic investigation in patients with underlying cirrhosis or chronic hepatitis B. Alpha-fetoprotein level may be a useful adjunct.
- Core biopsy is not routinely indicated for patients being considered for curative surgical resection or transplant. Biopsies should be carefully considered by a transplant team when patients are eligible for transplant.
- Core biopsy can be considered for those patients with noncurable disease who are eligible for systemic therapies, to confirm diagnosis and/or for research purposes.
- For nonsurgical patients with atypical radiologic findings, core biopsy may be useful.
Summary of discussion

The conference enjoyed a debate on the need to biopsy HCC to pathologically confirm the diagnosis. The "Pro" side was argued by Dr. Renata Peixoto, GI medical oncology fellow from the BC Cancer Agency, and the "Con" side was argued was Dr. Richard Semelka, diagnostic radiologist from the University of North Carolina in Chapel Hill.

The group was convinced by Dr. Semelka’s argument that most HCC can be reliably diagnosed with good cross-sectional imaging in a patient with appropriate risk factors (e.g. cirrhosis). Dr. Peixoto was equally convincing that biopsies in those with advanced disease are crucial in a research setting in order to better understand the molecular biology of this illness. The audience discussion echoed these two thoughts, and the medical oncologists in the group were comfortable prescribing systemic therapy based on a characteristic clinical diagnosis. It was also noted that biopsies in potential transplant patients should be done in consultation with the transplant team, as various centres will deem patients temporarily ineligible due to the risk of tumour spread from the biopsy itself.

References