



October 16, 2009

Dr. Steven D. Pearson
Director
Institute for Clinical and Economic Review
Massachusetts General Hospital
101 Merrimac Street, 10th Floor
Boston, MA 02114

Re: Comments on Management Options for Low-Risk Prostate Cancer: A Report on Comparative Effectiveness and Value

Dear Dr. Pearson:

The American Society for Radiation Oncology (ASTRO) appreciates the opportunity to participate in the work of the Institute for Clinical and Economic Review (ICER) by offering the following comments regarding the draft report entitled “Management Options for Low-Risk Prostate Cancer: A Report on Comparative Effectiveness and Value.”

ASTRO is the largest radiation oncology society in the world, with approximately 10,000 members who specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, biology and physics, the Society is dedicated to the advancement of the practice of radiation oncology by promoting excellence in patient care, providing opportunities for educational and professional development, promoting research and disseminating research results and representing radiation oncology in a rapidly evolving healthcare environment.

In general, ASTRO believes this draft report is a comprehensive review covering the majority of prospective and retrospective studies of outcomes after the management of prostate cancer. However, we would note that the evidence of comparative effectiveness in this disease is of fairly low quality, and we hope that this report does not overreach by suggesting a deeper level of understanding than exists. Additional research, particularly with regard to quality of life outcomes measures, is clearly needed.

We appreciate the significant work that was undertaken with this draft report and applaud your effort. At the same time, ASTRO believes it is important to comment on the specific limitations and biases in this draft report as several of the strongly delivered recommendations are based upon weak assumptions.

Bias Toward Active Surveillance.

We agree that Active Surveillance (AS) is an important management option that prostate cancer patients should consider. However, we are concerned that the Evidence Review Group may have given too much weight to the limited data on AS. While long term data is presented and

criticized on each treatment regimen, there exists no long term data on AS¹. We would note that there is hardly equivalent data in the follow up and case numbers for AS as there is for most other retrospective and prospective series. There may be insufficient data on AS until the completion of the START trial comparing surveillance to treatment; as noted on page 32, this trial is still accruing patients.

Risk Adjustment for Comorbidities

We are concerned that little attention is paid to the impact of co-morbid illnesses and disparate baseline values between modalities. As described in the Sanda NEJM paper (2008), the baseline data is very different for the three different modalities. The surgical patients, being younger, often have a baseline QOL that is superior to the external beam radiation therapy (EBRT) and brachytherapy (BT) cases. This analysis needs to further highlight the variation in prostate cancer patients and explain the risk adjustment methodology to hold constant the outcomes associated with each treatment.

Issues with the ICER model

ASTRO questions the assumption that men on AS will get radical prostatectomy (RP) if < 65 and IMRT if >65. Surely some of these men will choose BT. We believe the model should reflect BT as a possibility.

The model assumes that the risk of prostate cancer death is the same for AS and immediate treatment. We question this assumption, particularly since some patients will fail active surveillance. One would hope that the number of patients who fail active surveillance and become incurable is very small, but in our experience it is not zero. We believe the model should reflect slightly greater risk with AS since some patients will fail to follow up regularly.

Finally, we are wary of the assumption that no men treated with RP receive adjuvant EBRT. Several of the references listed are at least a decade old and three randomized trials showing an effect of post RP EBRT are not listed. Given the publication of these three studies, we believe at least some men will get EBRT after surgery. Anecdotally, we are hearing from our members that patients who choose robotic surgery are slightly more likely to have positive margins and this finding is validated by the Hu JCO paper (2008, attached).² Positive margins would also increase the likelihood of EBRT. We believe the model should reflect the possibility of EBRT post RP.

Issues with the CVE Table

ASTRO is concerned by the characterization of some clinical outcomes in the “Base Case” model. Specifically, the statement, “The risk of urinary incontinence is 9% with surgery, 7% with brachytherapy, 6% with IMRT, and 2% with proton beam therapy. Among the radiation modalities, the risk of proctitis ranges from 2% for brachytherapy to 10% for proton beam

¹ The Choo (2002) series of 206 patients had a 29 month median follow up and the Hardie (2007) series of 80 patients had a 42 month median follow up. Other than the Toronto series, most of these reports have median follow up of only 3.5 years.

² As noted in the draft report, this phenomenon may be related to the learning curve for surgeons becoming more familiar with this newer technique.

therapy.” The toxicity estimates identified in the draft report are hard to justify, especially the estimates for urinary incontinence. These numbers have no relationship to what patients describe (Sanda, NEJM 2008).

Review of Alternative Management Strategies

In its review of the management strategies for prostate cancer, we believe it should be further emphasized that while prostate BT is efficacious and with low cost, many patients may not be good candidates because their glands are too big. Of the radiation options, it is important to note that there are increased urinary toxicities for BT pts (*i.e.*, that is why patients with high AUA scores are not eligible) and fewer bowel issues compared with external beam where the urinary toxicities are fewer but there are more bowel changes.

Technical Questions / Corrections

- On page 5, in the summary of key findings, it states: “Radiation treatment has a higher rate of short and long-term bowel side effects than surgery, and, among radiation options, IMRT has a higher rate than brachytherapy.” We did not find data supporting this assertion in the body of the report.
- On page 22, in the description of the NCI (2006) guidelines on the use of IMRT, we believe the link is mischaracterized. The URL refers to a January 2005 NCI letter that did not intend to state the place of IMRT in clinical care so much as to define its place in clinical trials and standards for participation.
- On page 13, the report states “In the United States, IMRT has largely supplanted 3D-CRT...” While we tend to agree that this is probably true, a supporting reference would be appreciated.
- On page 15, the report states that brachytherapy “typically involves...an overnight hospital stay.” ASTRO is unclear whether an overnight stay is typical, or if patients are able to go home the same day of the implant. This is an area where there may be variation in practice. Again, a reference or supporting data would be useful.
- On page 15, the report states that brachytherapy is not indicated for patients with a large prostate. We agree with this statement; however, we believe the volume indicated (40cc) is too small. The RTOG study (RTOG 0019) used a 60cc cutoff for eligibility.

Conclusion

ASTRO appreciates the opportunity to provide comments on the draft report. We value the effort and expertise of the ICER staff and report authors and remain ready to work closely with ICER to improve the assessment of comparative effectiveness of various radiation oncology treatments. Please contact Emily Wilson at 703-839-7364 or emilyw@astro.org if you have any questions.

Sincerely,



Laura I. Thevenot
Chief Executive Officer