

MINUTES

Health Technology Assessment Subcommittee

Clackamas Community College Wilsonville Training Center

29353 SW Town Center Loop E

Wilsonville, OR 97070

June 11, 2015

1:00-4:00pm

Members Present: Som Saha, MD, MPH (Chair Pro Tempore); Jim MacKay, MD; Chris Labhart; Gerald Ahmann, MD; Mark Bradshaw, MD; Leda Garside, RN.

Members Absent: Tim Keenen, MD.

Staff Present: Darren Coffman; Cat Livingston, MD, MPH; Jason Gingerich.

Also Attending: Adam Obley, MD, Val King, MD, MPH, Robyn Liu, MD, MPH, and Aasta Thielke, OHSU Center for Evidence-based Policy; Troy Rayburn, American Cancer Society; Ronnie Castro, PORCH; Carl Rossi, Scripps; Carol Marquez, OHSU; Ramesh Rengan, Seattle Cancer Care Alliance; Stephen Holm, MD Anderson; Mark Pledger, Novartis.

1. CALL TO ORDER

Som Saha called the meeting of the Health Technology Assessment Subcommittee (HTAS) to order at 1:00 pm.

2. MINUTES REVIEW

Minutes from the February 18, 2015 meeting were approved as presented 6-0.

3. STAFF REPORT

Coffman reported on membership changes. Saha and Garside have joined the HTAS, and membership is now balanced with seven members on each subcommittee. Derrick Sorweide, DO, plans to join the subcommittee in September. King introduced Adam Obley, part of the clinical epidemiology staff at the Center for Evidence-based Policy. He will take over the work Robyn Liu has been doing in recent months. Coffman thanked Liu for her work. Wally Shaffer, who has served as clinical staff to the subcommittee, has retired and Cat Livingston will serve as staff to this subcommittee for the time being.

Coffman reported that the HERC is revising its coverage guidance process to perform additional work up front to prevent the starts and stops that have occurred on more complex topics in the past. We will also be more explicit about important versus critical outcomes as we report evidence, and are working on a revamped GRADE table which includes more specific outcome information when it is available. We will continue to use the GRADE domains including values and preferences, benefits and harms, resource allocation and strength of evidence. The

Coverage Guidance Development Framework (algorithm) has been retired as it has sometimes created confusion and unnecessary complexity. It served its purpose initially but GRADE has proven more useful.

4. BIOMARKER TESTS OF CANCER TISSUE FOR PROGNOSIS AND POTENTIAL RESPONSE TO TREATMENT

Liu reviewed the public comment disposition and staff suggested responses. For MSI for detecting Lynch Syndrome, Saha asked what the alternative test was and for the argument against clinical utility. Liu explained that IHC4 is available and that there are no studies showing MSI to have additional benefit on patient-centered outcomes. Saha asked whether it has better discriminating capacity. Liu said it does not. IHC4 is less costly.

Liu reviewed public comments and responses regarding Prolaris for Prostate Cancer. Saha said that he doesn't believe it's reasonable to hold such a diagnostic test to a standard of decreasing mortality as conducting such a trial would be almost impossible. The utility of the test could also reduced aggressive treatment. He is more interested in whether the test accurately predicts who needs therapy more than whether the test changes decisionmaking or mortality. Ahmann said the test isn't useful because if a man is told he has prostate cancer and is not too old for surgery, he is very likely to opt for surgery unless you can tell him that there is zero chance that the cancer will progress. Saha said a study showing that it would actually prevent surgery may be difficult to conduct. King noted that there were similar issues with Oncotype Dx for breast cancer; the evidence wasn't there a few years ago but now it is. There are competing tests for prostate cancer, and it remains to be seen which will obtain evidence of effectiveness in changing decision-making. She suggested that the subcommittee should revisit this test in two years to see whether the evidence develops. Livingston said that staff will shift the public comment disposition to focus on avoiding unnecessary care rather than mortality.

Saha offered an opportunity for public comment. Carol Marquez, a radiation oncologist at OHSU testified. She disclosed no conflicts of interest. Though she doesn't see prostate cancer patients, she said she has seen an evolution of cancer care in that some patients are now choosing to avoid invasive treatments because of concerns about quality of life and treatment side effects. Ahmann said that most prostate cancer patients are generally over 65, and that much of that generation is very fearful of cancer. Marquez noted that with PSA testing, prostate cancer is sometimes diagnosed earlier in life. Saha asked about cost. Coffman said that staff found data indicating the test costs about \$3,400. While acknowledging that the test could prevent some surgeries, Saha said that if the cost of the test were lower, it might not be such an issue as long as there were no potential harms.

Livingston noted that multiple molecular testing is not recommended for coverage, but there is no GRADE row for that. Staff will add one, reflecting the insufficient evidence reported in the body of the text, putting in the validity and utility if possible.

Livingston reviewed the changes to the GRADE table where staff listed the analytic validity, clinical validity or clinical utility. Rationale used to refer to the Coverage Guidance Development Framework (algorithm) which is no longer present. Therefore the rationales have been updated. Livingston reviewed the updated rationales. Saha asked that the definitions of the terms be defined as footnotes to the GRADE table.

The draft coverage guidance was approved for referral to VbBS and HERC with the changes

requested by the subcommittee.

DRAFT HERC COVERAGE GUIDANCE

Oncotype DX is recommended for coverage in early stage breast cancer when used to guide adjuvant chemotherapy treatment decisions for women who are lymph node negative (*strong recommendation*).

The following genetic tests of cancer tissue are recommended for coverage (*strong recommendation*):

- BRAF gene mutation testing for melanoma
- Epidermal growth factor receptor (EGFR) gene mutation testing for non-small-cell lung cancer
- KRAS gene mutation testing for colorectal cancer

The following genetic tests of cancer tissue are not recommended for coverage (*weak recommendation*):

- Mammaprint, ImmunoHistoChemistry 4 (IHC4), and Mammostrat for breast cancer
- Prolaris and Oncotype DX for prostate cancer
- BRAF, microsatellite instability (MSI), and Oncotype DX for colorectal cancer
- KRAS for lung cancer
- Urovysion for bladder cancer
- Oncotype DX for lymph node-positive breast cancer

The use of multiple molecular testing to select targeted cancer therapy is not recommended for coverage (*weak recommendation*).

5. INDICATIONS FOR PROTON BEAM THERAPY

Liu reviewed the public comment disposition and staff's recommended responses. She reviewed the comments by cancer type, using the groupings from page 56 of the meeting materials.

For brain and paraspinal tumors, Saha asked Liu about the results of the updated literature search. Liu said that the information about cognitive impact and quality of life was new, though the Washington HTA had already recommended coverage based on incremental net benefit, so she's not sure the additional evidence changes the assessment of evidence. For the benefit of the new members, Coffman noted that for this indication and pediatric tumors the subcommittee appeared to be on the fence about its recommendation at the last meeting. The subcommittee previously recommended against coverage but appeared open to changing the recommendation based on public comment. The balance of benefits and harms in the GRADE table has been changed to incremental benefits to match Table 1 of the coverage guidance. Livingston clarified the incremental benefit of the treatment is that there are fewer harms, not some other benefit. There is insufficient comparative evidence about survival or other cancer-related outcomes. Saha requested that staff separate the benefits of treating the cancer from the harms (side effects of treatment). After discussion the subcommittee agreed to make a weak recommendation for coverage related to brain and spinal tumors. Saha then asked about the

cost comparison. The cost is more than IMRT or photon therapy but only approximately twice as expensive (not 10 times more expensive).

For breast cancer, liver cancer and other gastrointestinal cancers the subcommittee made no change based on public comments after minimal discussion.

For head and neck cancers, Saha asked about the rate of local control with typical photon therapy. Liu referred him to comment L68 in which an error was discovered during discussion: the local control rate for skull based tumors with photon therapy is 30-50%, not 3-5% as shown in the disposition document. After brief discussion, the subcommittee decided to recommend coverage for some, but not all, head and neck tumors. After discussion, including testimony and clarification from radiation oncologists Marquez and Rossi, who were in the audience, the subcommittee decided to recommend coverage for brain, skull-based and juxtaspinal and paranasal sinus tumors based on the evidence cited in the public comment disposition. As these are rarer tumors, the subcommittee chose to recommend coverage based on lower-quality evidence which shows better outcomes than is typical with standard therapies.

For nasopharyngeal and oropharyngeal carcinoma, the subcommittee discussed that these tissues are more radiosensitive but also sensitive to chemotherapy. Marquez said that because the tumors are more radiosensitive, there may not be as much benefit of proton therapy over photons. Rengan agreed that they are sensitive to chemotherapy but said that radiation therapy is needed for a cure, and added that for more sensitive tumors the benefit would be the ability to safely increase the dose to the tumor, rather than reduced harms. Rossi said that proton beam centers have only recently developed the ability to target these tumors due to improved technology. After discussion, the subcommittee decided not to recommend coverage for these tumor types, based on insufficient evidence of superiority and the fact that these tumors are common enough that one might expect future evidence development.

In discussion of retreatment, Ahmann asked if people who were retreated were ever cured. A member of the audience said sometimes yes, but often treatment is to improve quality of life or to extend life. The audience member said that these are difficult decisions and depend on the characteristics of each patient. Ahmann noted that treatment of recurrent tumors would significantly differ depending on their location. Saha suggested they are rare enough not to include a restriction for them, so perhaps the subcommittee could remain silent. However in subsequent discussion, Rengan noted that there is a blanket recommendation for all other conditions which could be interpreted as a recommendation of noncoverage for retreatments. Livingston agreed to look into clarifying language around this issue.

Saha asked about liver cancer. Liu reviewed the evidence from the public comments and the cited Chi study. The reported five-year survival benefit was 25 times higher in the proton population, with less dramatic benefits at shorter time horizons. Benefits were, however, similar to stereotactic body radiation therapy (SBRT). Gingerich noted that HERC recently elected not to cover SBRT for liver cancer. Harms of proton therapy were reported as less serious than either SBRT or standard photon radiation, though harms were just general hepatic toxicity, which Saha said are not important as an outcome. Upon further research into this article, King found indications of heterogeneity (high i^2 values) that call these results into question. The subcommittee did not change its recommendation.

Discussion turned to pediatric cancers. Most of the comments on pediatric cancers were for eye, head and neck cancers, which would already be recommended for coverage regardless of age per previous discussion, so the subcommittee did not discuss the comments related to

these cancers. For lymphomas and Ewing sarcomas, Marquez noted that many Ewing Sarcomas occur in the juxtaspinal region. Saha asked about the intent of separating out pediatric and adult tumors. Staff responded that toxicity will develop over decades, so long-term outcomes are more important because children typically have more life expectancy. Rengan said that treatment-related secondary malignancies can appear decades after primary treatment, and that children's tissue is more radiosensitive than adult tissue. Based on these factors, the subcommittee decided to make a weak recommend for coverage for all tumors that occur in children.

Saha invited additional public comments.

Ronnie Castro, of Seattle, offered comment as a patient. He had a skull-based brain tumor, diagnosed in 2013 at age 32. After six months, he was able to raise private funds for proton beam therapy despite an insurance denial and the tumor has not grown again. He wondered what would have happened if he had not been able to raise the money and expressed concern about long-term harms, which may have occurred with photon therapy. He expressed satisfaction at the subcommittee's decision to recommend coverage for these cancers.

Rengan gave a brief presentation focusing on the deleterious effects of radiation exposure to normal tissue. He also said that toxicity of therapy creates costs to the health system. In many cases this creates savings which compensate for the additional cost of proton-based therapies.

Livingston then asked for guidance on completing the next draft for the September meeting. After discussion the subcommittee decided that nasopharyngeal and oropharyngeal carcinoma would remain recommended for noncoverage, and that brain, skull based, juxtaspinal and paranasal sinus tumors would be given a separate row with a weak recommendation for coverage. Rare tumors will not get a separate row on the GRADE table. Malignant pediatric cancers (including lymphoma) will have their own GRADE row with a recommendation for coverage. Staff will research the thinking behind the varied definitions of pediatric, with age limits of 21 and 30 in different sources.

Saha thanked the members of the audience for their testimony and assistance with the coverage guidance and invited them to call in by phone to the next meeting. Prostate cancer, lung cancer and adult lymphoma will be the main areas of interest.

6. NEXT TOPICS

At the next meeting the subcommittee will continue discussion on proton beam therapy and take up a new topic related to bariatric and metabolic surgery.

7. ADJOURNMENT

The meeting was adjourned at 4:10 pm. The next meeting is scheduled for September 10, 2015 from 1:00-4:00 pm in Room 155 of the Clackamas Community College Wilsonville Training Center.