

RRP Task Force 2018 Spring Meeting - Highlights
19 Apr 2018 Meeting – Gaylord National Harbor Hotel, Maryland

The meeting began with a short introduction of those attending which included RRP Foundation representatives: Kim McClellan, Marcelle Stiff, Maura Burke Weiner, Vicki Treanor, Elizabeth Volz, Stephanie Woo, Marlene and Bill Stern

Summary of RRP/HPV events, RRP presentations at COSM, Otolaryngology societies RRP grants:

- First International HPV awareness day was March 4, 2018.
- ESPO: Stockholm, Sweden June 2-5, 2018. Not certain who is running the RRP session
- International HPV meeting: RRP and Head and Neck Cancer Satellite Workshops will take place at next meeting in Sydney, Australia in October 2-6, 2018.
- EUROGIN, Lisbon, Portugal, December 2-5, 2018: RRP session being organized by Simon Best.
- 1st World Congress in Pediatric Otolaryngology Buenos Aires, Argentina April 7-10, 2019. Craig Derkay to moderate session.
- Two posters as part of COSM: B021 RRP and Radiation therapy; H051 Avastin case report
- ABEA/ALA RRP Panel on Friday April 19: Moderated by Gaelyn Garrett, Talks by Craig Derkay, Simon Best and Clint Allen: RRP RIP?
- Core grant approved by ASPO Board 2017:
Prosser, Cincinnati, “Characterizing xenograft models of recurrent respiratory papillomatosis” (\$19,976)
- Core grant approved by AAO-HNS:
David Lee, Cincinnati, “Genetic susceptibility of RRP to adjuvant therapy”

Key topics discussed of relevance to the RRP patient community:

Gardasil 9:

- Merck stopped making the 4-valent vaccine after December 31, 2017.
- If already vaccinated with 4-valent vaccine it is recommended not to re-vaccinate with 9-valent.
- New CDC recommendation is to use two-dose schedule for Gardasil 9 (instead of previous 3 doses for Gardasil 4). As of 2016 in the US ~60% compliance for single dose but poorer for 2 doses. (Much greater compliance in many other countries, such as Australia, UK, Northern Europe and Canada.)

Avastin:

- Avastin is believed to be a suppressant for RRP, but not likely a cure.
- There is a need to understand how various providers administer Avastin. There's a need to develop a protocol.
- Should intralesional Avastin be introduced early as an adjunctive therapy? Dr. Pransky is using it in this way and Dr. Derkay suggests a trial to see impact of Avastin as "first line" therapy.

Systemic Avastin:

- Need to create a database where providers using this therapy provide data on their patients' responses/dosing/schedule/adverse events.
- MD's present who say they are currently using systemic Avastin include: Dr. Simon Best (JH), Dr. Adam Klein (Emory), Dr. Douglas Sidell (Stanford), Dr. Karen Zur (CHOP), Dr. Nazaneen Grant (Georgetown).
- Question is which population should this be used on, and what is the best course of dosage into maintenance. (Dr. Best updated this conversation on Friday during the RRP Panel Discussion.)
- Dr. Derkay mentioned the high patient load in Beijing, China and wondered if that would be the best location to run a study using systemic Avastin on a larger patient pool.

Adjunct Therapy:

- There was a fairly robust debate on the timing of adjunct intervention, as well as differing thoughts on Gardasil 9 on currently already active RRP patients.
- Gardasil for treatment: Despite a difference of opinion on whether it might prevent regrowth, the RRP task force endorses the use of the vaccine even prior to age 9 in affected children, with little down-side. RRP doctors are encouraged to note which patients are given the vaccine in this fashion for possible future collaborative retrospective study. In most cases the vaccine is being given to many JORRP patients while in the OR without any insurance issues. Dr. Derkay mentioned that about a 50% appear to respond after given the vaccine. So there seems to be a consensus that it won't hurt to give the Gardasil 9, and until we can get a randomized clinical trial approved and running, it's still the best course of action.
- Cidofovir did not get the same level of conversation as seen in other task force meetings-it seems many providers are going more towards Avastin.
- The most looming question from this adjunct therapy conversation was whether adjunct treatment should be introduced early in the disease process, before it becomes an aggressive case. (This included the possible use of systemic Avastin.) In this regard, Dr. Derkay said, "I'd rather give my child three infusions a year, compared to three OR procedures a year."

Clinical Trials - Updates:

- Dr. Clint Allen-NIH: Avelumab (Anti PD-1), in process of completing trial and awaiting approval to publish.

- Dr. Clint Allen-NIH: New trial, using Avelumab and a Beta Trap, should be enrolling within three months. (More info in RRP Panel Discussion report)
- Dr. Allen's lab, which does more than RRP, just received a 10M Cancer Moonshot grant to design T-cells to target different antigens. Could have many applications, including RRP.
- Dr. Sarah Pai, Dr. Friedman-Mass General (Boston)/Northshore (Evanston, IL): Keytruda (Anti-PD-1), 15/21 enrolled, age range is now 12 and up, two year commitment, funded by Merck, currently no travel funds available. Currently an FDA review is occurring.

CDC Study Update:

- Vidisha Singh (and Elissa Meites remotely) presented the preliminary results of the prospective study with an abstract recently submitted for the International HPV meeting in Sydney. 127 JORRP patients studied retrospectively with a median diagnosis age of 3 and a median current age of 22 showed 90% were vaginally born from young unvaccinated mothers. 80+% of cases involved HPV type 6 and 11% of cases involved HPV type 11 (which appears to be associated with more involvement below the trachea). Also, prospective part of study is suggesting a decline in new RRP cases. Specifically, Australian data is showing a significant decline in cases of RRP as a result of their HPV vaccine program.

Tissue banks and progress in growing papillomas in vitro for "personalized medicine"/drug testing:

- Desire to learn from each other to improve survival of cell lines.
- Dr. Adam Klein's tissue bank at Emory
- Dr. Chris Hartnick at Mass Eye and Ear coordinating with Novartis about possibility of performing outside testing.
- Dr. Seth Pransky and Dr. Matt Brigger at San Diego
- Dr. Richard Schlegel in DC creating an immortalized cell line for personalized drug testing.

RRP Genetics Study Update:

- Dr. Buchinsky continues to work with colleagues at NCI and University of Pittsburgh to perform whole genome sequencing on specimens. Seeking additional Bioinformatics assistance.

Pulmonary RRP Working Group report - RRPF:

- The RRPF came in front of the RRP task force asking for a focus on pulmonary RRP. (Handouts, minus the excel patient sheet were made available to doctors attending.) RRPF Pulmonary was able to collect data on thirty pulmonary patients via social media/referral contact, as well as gather data on patients via informal FB polls. The presentation (by Marcelle Stiff) included information from Jennifer Woo's presentation on pulmonary RRP at the 2014 RRP meeting at Johns Hopkins.

- The RRPF current pulmonary working team includes: Susan Woo, Marcelle Stiff, Kim McClellan. Elizabeth Volz was brought in by Marcelle and Kim to assist in preparing the presentation. (There was more conversation on this topic during Friday's RRP panel discussion.)
- Dr. Derkay agreed that the Task Force could assist in finding a center willing to gather data from centers on their patients/treatments/outcomes to better serve the pulmonary RRP community as well as get a better understanding of the actual % of RRP patients who do have pulmonary metastasis.
- RRPF, Marcelle Stiff, mentioned that centers often do have multiple patients, but without a centralized, organized team at that facility, there is no conversation between medical providers on treatment/outcome/risk factors.
- If you have any information on pulmonary patients that we do not have, please share that information with Marcelle or Kim.
- The RRPF is proposing to add a more detailed pulmonary section to the RRPF survey.
- As part of the Pulmonary Papilloma Research Initiative, during the second half of 2018 the RRPF will be issuing a RFP with the goal of awarding a grant of up to \$50K in funding towards promising pulmonary RRP research studies.

New ideas for RRP Task Force research initiatives and other new business:

- Creating treatment guidelines and regional resources regarding treatment of RRP patients with pulmonary disease: May be an opportunity to utilize RRPF survey/database to learn more about these patients. Also, may be an opportunity for a PICORI grant. RRP Task Force members interested in working with the RRPF on this project are asked to identify themselves to Dr. Derkay/Bill Stern and/or Kim McClellan (themcclellanfamily@comcast.net) and/or Marcelle Stiff (marcellestiff@comcast.net). Dr. Derkay will try and form a working group to address these questions.
- FDA Proposes Off-Label Standards for Drug, Device Promotion - This may allow communication to Pediatricians and Family Practitioners regarding the potential benefits of HPV vaccination in preventing RRP and Oro-pharyngeal cancers!

Next RRP Task Force meeting: Will take place in conjunction with the 2018 annual AAO-HNS meeting. It is tentatively scheduled for Saturday October 6, 2018. Due to a likely lengthy agenda associated with many new developments, the meeting time is proposed to be extended to 90 minutes.