Supplemental Data:

1. Survey with email introduction

Dear RI's,

With the conclusion of the two randomized trials investigating the use of sodium thiosulfate (STS) to prevent or mitigate hearing loss from the chemotherapy agent cisplatin, the COG Cancer Control & Supportive Care Committee is exploring a new concept for a successor trial in hearing protection. We are therefore looking to better understand current views within the oncology community whether STS should be considered the standard of care in cisplatin treated patients, enthusiasm for a potential successor trial, and approaches to hearing monitoring and dose modifications from cisplatin-induced hearing loss.

If you feel someone at your institution is best suited to answer questions on cisplatin and hearing loss, please forward the below link.

The survey will take approximately ten minutes to complete.

We are hoping to discuss at the Spring Meeting March 12-14. If possible, it would be great to have the survey completed beforehand

https://www.surveymonkey.com/r/MHKYTYQ

Thank you for your insights and engagement with the CCL committee.

1. Name of institution:

Cisplatin-Induced Hearing Loss

General Description of Institution

Please provide an estimate for how many of each tumor your institution begins therapy for each year (i.e. new diagnoses).

2. At your institution, approximately how many new patients are diagnosed each year with:

Medulloblastoma	
Osteosarcoma	
Liver Tumors (Hepatoblastoma or Hepatocellular Carcinoma)	
Germ cell tumor	
Neuroblastoma	

3. At your institution, approximately how many new patients start therapy with a cisplatin-containing regimen each year (i.e cisplatin therapy for ANY type of tumor):

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ROUTINE USE OF SODIUM THIOSULFATE (STS)

Following the recent publications describing partial hearing protection from the incorporation of Sodium Thiosulfate (STS) into therapy on the randomized trials ACCL0431 (Freyer et al Lancet Oncology 2017) and SIOPEL6 (Brock et al New Engl J Med 2018):

4. Does your institution CURRENTLY or have FUTURE PLANS to ROUTINELY incorporate STS into cisplatin-based therapy for hearing protection?

- ◯ Yes
- ◯ No

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YES, WE ROUTINELY USE STS OR HAVE PLANS TO DO SO

5. Who will **ROUTINELY** receive STS as part of their cisplatin-based therapy? STS will be provided to patients with: **Check all that apply**

	Localized tumors	Disseminated tumors
Medulloblastoma	☐	☐
Other brain tumors	☐	☐
Osteosarcoma	☐	☐
Hepatoblastoma	☐	☐
Hepatocellular carcinoma	☐	☐
Germ Cell Tumor	☐	☐
Nasopharyngeal carcinoma	☐	☐
Other cisplatin-treated tumor	☐	☐

Other (please specify)

6. **Separate from "disease dissemination**," are there **OTHER** criteria that are or will be used to determine who will ROUTINELY receive STS for hearing protection **(e.g. high vs low risk tumor, # of cisplatin days, etc)**?

7. Should a future prospective research trial become available for hearing protection in **LOCALIZED DISEASE**, would your institution be open to a control arm **WITHOUT STS** (i.e. observation only)?

- [ ] Yes
- [ ] No

Please share any additional insights into selection of a CONTROL arm for a future hearing protection trial:

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NO, WE HAVE NO PLANS TO ROUTINELY USE STS

8. What will determine potential future **ROUTINE** use of STS?

9. Should a future prospective research trial become available for hearing protection in **LOCALIZED DISEASE**, would your institution be open to a control arm **WITH STS?**

- ( ) Yes
- ( ) No

Please share any additional insights into selection of a CONTROL arm for a future hearing protection trial:

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FUTURE TRIALS IN CISPLATIN-INDUCED HEARING LOSS

Please answer the prevailing outlook at your institution toward potential future COG trials in hearing protection.

10. With the recent prospective trials ACCL0431 and SIOPEL6 establishing “proof-of-principle” for hearing protection, would your institution be interested in a **new research trial in hearing protection** for cisplatin-treated patients with **localized disease**?

- ◯ Yes
- ◯ No

Why or Why Not?

11. In the FUTURE, would a study involving trans-tympanic injections of a hearing protection agent with sedation be MORE or LESS attractive to your institution than a systemic hearing protection agent (pick the statement that best reflects the general viewpoint at your institution)?

- ◯ A study using trans-tympanic injections is **MORE** attractive than a study of a systemic agent?
- ◯ A study using trans-tympanic injections is **LESS** attractive than a study of a systemic agent?

Why?

12. If this FUTURE research trial investigating transympanic injections was proposed, would your institution likely be interested in opening it in:

- ◯ Localized disease only
- ◯ Disseminated disease only
- ◯ Any cisplatin-treated patient

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HEARING ASSESSMENTS FOR CISPLATIN THERAPY

Please help us understand how hearing is assessed at your institution for patients receiving cisplatin therapy.

We recognize there may be significant variability between providers, disease groups, protocols, etc. Where not specifically stated, please fill in the answer that <u>best fits</u> for <u>the majority</u> of cisplatin-treated patients.

13. What percentage of patients do you estimate receive routine baseline audiology screening prior to first cisplatin dose?

- ◯ None
- ◯ 25%
- ◯ 50%
- ◯ 75%
- ◯ Everyone

14. Do your refer patients for hearing assessments differently according to the **AGE** of the patient (e.g. assess hearing more or less frequently in an infant or younger child versus an older child or adolescent)?

- ◯ Yes (age is a consideration for timing or frequency of assessments)
- ◯ No (all patients are assessed the same)

**** IF YES, how is age considered for timing or frequency of hearing assessments:**

15. In general when do you assess hearing for cisplatin-treated patients? (check ALL that apply)

- ☐ Prior to START of any treatment (radiation and/or non-cisplatin chemotherapy)
- ☐ Prior to FIRST dose of cisplatin
- ☐ Prior to EVERY dose of cisplatin
- ☐ Prior to SOME doses of cisplatin (e.g. every 200mg/m2, every other cycle, etc)
- ☐ Prior to hematopoietic stem cell transplantation (HSCT) [if applicable]
- ☐ At end of therapy

If hearing is only assessed at set intervals, please describe:

16. Is the timing of routine hearing assessments different for those enrolled on a COG study versus those not enrolled on a COG study?

- ◯ Yes
- ◯ No

****IF YES, please describe the differences:**

HIGH-FREQUENCY AUDIOMETRY

High-frequency audiometry refers to audiograms that report hearing thresholds for frequencies >8,000 hz.

17. If high-frequency audiometry is available at your institution, would you factor hearing loss at the HIGHEST ranges (>8,000 Hz) into treatment decisions for adjusting cisplatin dosing?

- [ ] Yes
- [ ] I'm not sure
- [ ] No

****IF YES, briefly describe how:**

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DISTORTION-PRODUCT OTO-ACOUSTIC EMISSIONS (DP-OAE)

Distortion-product oto-acoustic emission (DP-OAE) are used to measure the physiologic function of the inner ear, and specifically, whether the outer hair cell remains functional following cisplatin-exposure.

18. If DP-OAE testing is available at your institution, would you factor DP-OAE results into treatment decisions for adjusting cisplatin dosing?

- ( ) Yes, loss of DPOAE at "speech" frequencies would affect my treatment decisions.
- ( ) I'm not sure
- ( ) No, I don't consider DPOAE even at "speech" frequencies in my treatment decisions

****IF YES, please briefly describe:**

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SPEECH AUDIOMETRY

Speech audiometry refers to testing by the audiologist of the ability to understand words or speech in silence and with competing noise. This testing simulates the "every-day" impact of hearing deficits.

19. If speech audiometry is available at your institution, would you factor deficits found ALSO on speech audiometry as compared to hearing loss seen ONLY on an audiogram into treatment decisions for cisplatin dosing?

- ◯ Yes, deficits found also on speech audiometry WOULD influence treatment decisions compared to hearing loss seen ONLY on an audiogram
- ◯ I am NOT SURE if I would factor speech audiometry into treatment decisions
- ◯ No, deficits found also on speech audiometry WOULD NOT influence treatment decisions compared to hearing loss seen only on an audiogram

Other (please specify)

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THANK YOU!

This completes the survey.

Thank you for your insights and for taking the time to complete these questions. The information gained will be used to aid planning for future research proposals to investigate strategies to mitigate hearing loss in children receiving cisplatin-based therapy.