ACTIVITY AND SAFETY OF TRANSDERMAL GRANISETRON IN PREVENTING NAUSEA/VOMITING INDUCED BY CISPLATIN AND RADIOTHERAPY IN HEAD AND NECK CANCER PATIENTS

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ABSTRACT

Introduction. Head and neck cancer (HNC) patients (pts) treated with concurrent chemo-radiotherapy (CRT) suffer from nausea and vomiting, induced by the synergistic effect of both modalities (CINV/RINV). Such symptoms affect pts health, quality of life (QoL) and compliance to cancer therapy.

Methods. This is a phase II, open-label, single-arm, prospective, multicentre trial, aimed to assess transdermal granisetron (GTDS) in preventing CINV/RINV and impact on QoL of in HNC pts candidates to IMRT with concomitant 3-weekly cisplatin (> 70 mg/m2 q3w). Adverse events (AEs) were collected according to CTCAE v5.0. For the whole treatment duration (7 weeks, wks), pts were asked to fill in daily the Nausea and Vomit Diary (NVD), reporting nausea intensity on a VAS scale; NV control was considered complete if VAS < 25 mm, with no vomiting and no rescue treatment (historical data = 5% of NV complete control). MDASI HN questionnaire was administered weekly.

Results. Among 68 pts enrolled, 11 did not apply GTDS and 13 filled in less than 7 days of NVD; 44 pts filled in ≥ 1 NVD wk (intention-to-treat population, ITT), and 30 had ≥ 4 NVD wks (compliant population) (fig. 1). 4 AEs (2 constipation, 1 dry mouth, 1 dysgeusia) were deemed potentially related to GTDS, none of grade >2. Complete NV control was reached in 25% and 26% in ITT and compliant population, respectively; rescue treatment was used in 56.8% and 51.6% cases by ITT and compliant population, respectively. According to MDASI HN questionnaire, cancer-related symptoms, HNC specific symptoms, and QoL interference significatively increased from wk 4, and peaked by wks 6-8.

Conclusions. GTDS is safe and seems to be more active in preventing CINV/RINV in HNC pts undergoing IMRT with concomitant cisplatin in regard to historical data. Its transdermal use may improve pt compliance. Results obtained from patient-reported outcome questionnaires provide a prospective library of pts symptoms during CRT.

Should you want more information about the study, feel free to contact us:
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INTRODUCTION

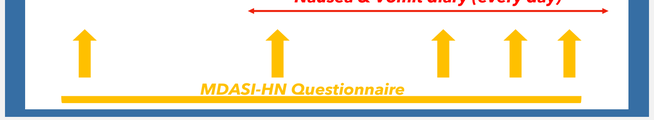
- **50-80% of pts undergoing concurrent CRT for H&N cancers suffer from** Chemo-Radiotherapy Induced Nausea/Vomiting (**C-RINV**)[1]
- **C-RINV is a relevant toxicity** affecting pt QoL, performance status, RT schedule and therefore treatment outcomes[2]
- **2023** updated **MASCC-ESMO Antiemetics Consensus**[3,4]:

Type of treatment	Emesis risk	Antiemetic Therapy recommended
Radiotherapy on H&N area	Low risk	• No prophylaxis • Rescue with DEX, dopamine RA, 5-HT3-RA
Intravenous Cisplatin	High risk	• Acute CINV: 4-drug single dose regimen (5-HT3-RA + DEX + NK1-RA + Olanz) • Delayed CINV: DEX +/- Olanz on days 2-4

PATIENTS AND METHODS

- A **phase II, prospective, open-label, single-arm, multicenter** (12 Italian centers), **investigator-initiated trial** (promoted by Italian GONO).
- **Study population**:
  - Age > 18 years old
  - Histologically-confirmed diagnosis of H&N primary (included CUP, nasopharynx, sinonasal and salivary glands)
  - Planned H&N area IMRT with concomitant 3-weekly cisplatin (3 cycles at > 70 mg/m^2 each)
  - No previous chemotherapy or previous RT on abdomen/brain
  - No emesis or significative nausea before CCRT start
  - No active use of cannabinoids.
- **Study design**: from week 4 to 8, addition of transdermal granisetron (GTDS) to standard antiemetics to improve nausea and vomiting control.

Treatment protocol (weeks)							
1st	2nd	3rd	4th	5th	6th	7th	8th
IV 5HT3							
CDDP			CDDP			CDDP	
NK1 ant			NK1 ant			NK1 ant	
Dex			Dex			Dex	
			GTDS->	GTDS->	GTDS->	GTDS-> GTDS	



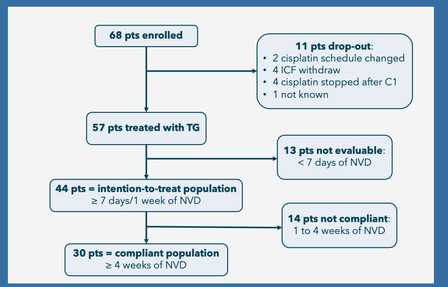
OBJECTIVES, ENDPOINTS AND SAMPLE SIZE

	Objective	Endpoint
1ry	**Activity** of GTDS in preventing C-RINV	**Rate of complete nausea/vomiting control**, defined as nausea VAS < 25 mm, no vomiting, no rescue antiemetic drugs taken
2ry	**Safety** of GTDS	Rate of treatment-related adverse events (**TRAES**)
2ry	Patient-reported outcomes (**PROs**)	• **MDASI-HN** scoring at weeks 1-4-6-7-8 • *(PRO-CTCAE via online app)*

- Complete nausea/vomiting control: H_0 in 5% pts[5] vs H_1 in 20% pts
- ∂ = 0.05, ß = 80%, attrition rate = 10%
- According to Green-Dahlberg study design: **sample size = 88 pts**

RESULTS

- **CONSORT** Diagram:



- **Complete nausea/vomiting control** reached by **25% and 26%** in intention-to-treat **(ITT) and compliant population**, respectively; **rescue treatment used by 57% and 52% in ITT and compliant population**
- **4 TRAEs reported**: 2 constipation, 1 dry mouth, 1 dysgeusia (**all G≤2**)
- **MDASI HN**, divided into 3 domains:

Cancer-related symptoms

HNC-specific symptoms

Interference with Quality of Live

DISCUSSION

- **GTDS seems more active in preventing C-RINV** in pts undergoing concurrent CRT for HNC **compared to historical control** when 5-HT3-RA were given only on day 1 for prophylaxis.
- **Poor compliance by patients to Nausea/Vomiting Diary**: only 30 pts out of 68 (44%) filled in at least 4 weeks out of 5 (80%) of the diary. However, no apparent difference between ITT and compliant population in terms of complete nausea/vomiting control and usage of rescue treatment was observed.
- **GTDS is safe**: few TRAEs reported, none G≥3.
- **MDASI-HN assessment during CRT provides a prospective library of pts symptoms during treatment**: all domains (cancer-related symptoms, HNC-specific symptoms, and QoL interference) significatively increased from week 4 and peaked by week 6 without further worsening.
- PRO-CTCAE analysis is still ongoing and will provide us more insights about pts self-reported symptoms.

CONCLUSIONS

- **GTDS is safe and may represent an option** to improve patient's compliance in preventing C-RINV related to concurrent CRT in HNC
- Nausea is more frequent than vomit but less responsive to TG, and this may be hypothesis generating for new trials
- PROs collection provide a prospective library of symptoms which may help pts and clinicians to improve treatment compliance and so outcomes.

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