

Healthcare resource utilization (HRU) survey to inform HRU data collection alongside the double blinded TrilynX study evaluating xevinapant in combination with chemoradiotherapy versus placebo plus chemoradiotherapy in patients with previously untreated locally advanced squamous cell carcinoma of the head and neck (LA SCCHN)

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Background and Objectives

- Head and neck cancers are the sixth most common cancer type, with 180,000 deaths worldwide in 2018 [1]. Over 50% of the patients with locally advanced head and neck cancer relapse after standard of care (SOC) [2]. High dose (100mg/m² Q3W) chemoradiation therapy (CRT) represents the SOC for locally advanced squamous cell carcinoma of the head and neck (SCCHN) [3, 4].

Survival rates vary significantly depending on anatomical site, stage, and human papillomavirus (HPV) status [5].

Head and neck cancer is one of the most debilitating types of cancer due to the impact the disease and available treatments exert on quality of life and patients' impairment in chewing, swallowing, and breathing [6-8]. The economic burden associated with SCCHN is substantial and was estimated at 3.64 billion USD in direct medical costs in 2010 in the United States [9].

- Head and neck cancers are regarded as resource intensive. There are limited data available though on healthcare resource use (HRU) and costs associated with SCCHN; most studies are based on selected SCCHN cancer types or patients within a few institutions with limited follow-up [4,6]. Hence, additional, and detailed HRU data are necessary.
- Xevinapant, a first-in-class oral Inhibitor of Apoptosis Proteins (IAP) with the potential to enhance the antitumour activity of chemotherapy and radiotherapy, is currently investigated in the Phase 3 TrilynX study (NCT04459715). HRU data is being collected alongside this trial as an exploratory endpoint and will be recorded by sites into the TrilynX electronic case report forms (eCRF).

Methods

A survey of 11 key questions was distributed to 20 Principal Investigators (PIs) participating in the TrilynX study.

The objectives were to:

- Determine the relevance of the HRU items to routine care while on trial
- Ensure items are understandable (in English)
- Provide recommendations for the study protocol and the electronic case report form (eCRF)

High-cost HRU items were prioritized and included:

- Inpatient hospitalizations (including intensive care unit [ICU] stays)
- Specialist consultation visits
- Diagnostic procedures
- Surgical procedures
- Nutrition-related procedures

For specialist consultation visits that were deemed relevant, the setting (in- and/or outpatient) and frequency was requested. Similarly, for diagnostic procedures that were deemed relevant, the frequency was requested.

Primary care and community care (e.g., general practitioner visits) as well as direct non-medical and indirect costs were not included.

Countries included: Australia, Austria, Belgium, Brazil, Canada, England, France, Germany, Greece, Hong Kong, Hungary, Israel, Poland, Russia, South Korea, Spain, Switzerland, Taiwan, Ukraine, and the US

Results

Ten of the twenty PIs responded.

Table 1 summarizes the relevance and suggestions from respondents. Radiology ward was deemed least relevant. Rewording recommendations are described.

Table 1. Inpatient hospitalization items

Item	PIs (n=10) supporting relevance	Rewording suggestions (country)
General (medicine/medical) ward	8	Medical ward (Greece) Internal medicine (Hungary)
Medical oncology ward	9	
Otorhinolaryngology ward	8	ENT ward (Australia, Hungary) Head and Neck Surgery (Hungary)
Radiology ward	4	Radiology department (Greece, Hungary)
Surgical ward	8	N/A
Rehabilitation ward	10	N/A
ICU	10	N/A
Hospice/palliative care ward	9	N/A

All specialists listed including visits to a specialist for tube placement for nutrition were deemed relevant by 8 of 10 PIs except for occupational therapist (4/10), surgical oncologist (7/10) and clinical nurse (7/10). For relevant specialist visits, KOLs indicated the setting (in- and/or outpatient) (Figure 1) and how often a patient would see this specialist in a year (Figure 2). In **Figure 1**, most specialists visits are performed in both the in- and out-patient setting except for dental visits, dietician visits, and social worker visits. There was wide variability in the frequency of specialist visits as reported by the KOLs (Figure 2) with visits to oncologists, radiologists, radiation oncologists, ear nose and throat specialists and nurses occurring most frequently (> 3 times per year).

Figure 1. Setting (inpatient / outpatient) of specialist visits

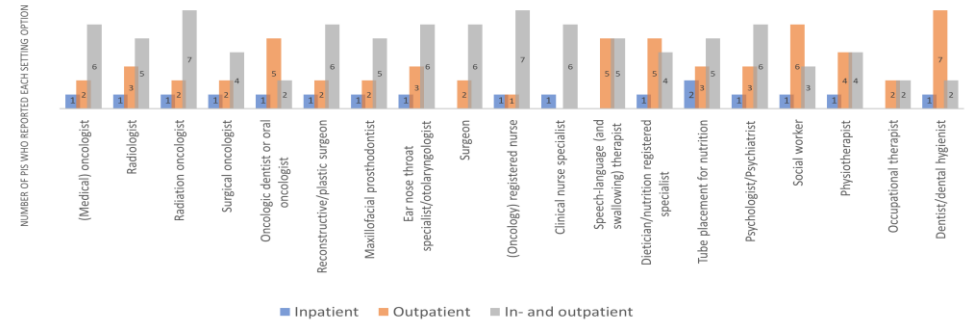
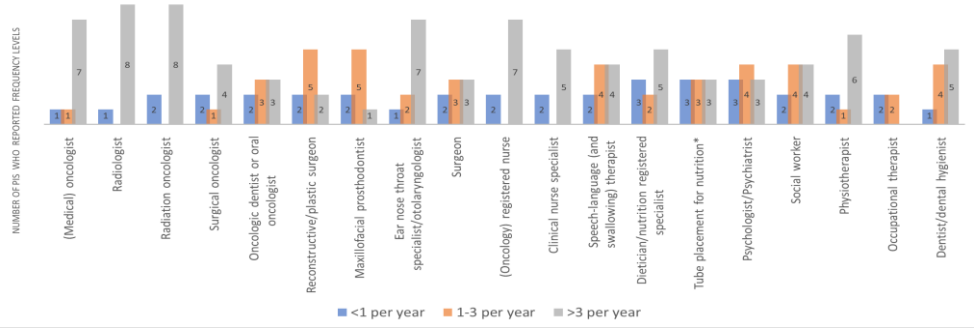


Figure 2. Annual frequency of specialist visits



As shown in **Table 2**, all diagnostic investigations except PET scans were deemed relevant by at least 8 of the 10 PIs, with no rewording of items suggested and one addition proposed (US guided core biopsy). KOLs reported that the majority of diagnostic interventions occurred 1-3 times per year (**Figure 3**).

Figure 3. Frequency of diagnostic investigations

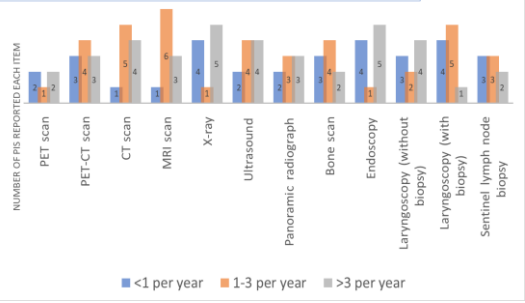


Table 2. Diagnostic investigation items (relevance)

Item	PIs (n=10) supporting relevance
PET scan	5
PET-CT scan	10
CT scan	10
MRI scan	10
X-ray	10
Ultrasound	10
Panoramic radiograph	8
Bone scan	9
Endoscopy	10
Laryngoscopy (without biopsy)	9
Laryngoscopy (with biopsy)	10
Sentinel lymph node biopsy	8
Other	US guided core biopsy

Conclusions

- Direct hospital-based treatment costs are a main cost driver therefore excluding costs in the primary care and community care setting has minimal impact on understanding total HRU.
- Societal costs are also regarded a cost driver for head and neck cancer (e.g. productivity losses attributable to work absence) and should be assessed to have a more complete picture of HRU.
- A pre-study HRU survey among PIs informed relevant resource utilization to be considered as part of data collection within the TrilynX trial. Adaptations were made based upon this feedback to the study protocol and eCRF. This will ensure a comprehensive overview of relevant HRU for SCCHN patients.
- This information will help inform payers on the costs associated with SCCHN in the context of xevinapant treatment and can be used to inform cost effectiveness and budget impact analyses.

References

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Table 3: Surgery (resection and reconstruction) items: relevance

Item	PIs (n = 10) supporting relevance
Laryngectomy - total	9
Laryngectomy - partial	10
Hemilaryngectomy	10
Microlaryngoscopy	10
Laryngopharyngectomy - total	10
Laryngopharyngectomy - partial	10
Pharyngectomy – total	9
Pharyngectomy - partial	10
Mandibulectomy - total	9
Mandibulectomy - partial	9
Tracheostomy/tracheotomy	10
Elective neck dissection (END)	10
Therapeutic neck dissection	8*
Minimally invasive or endoscopic head and neck surgery	10
Laryngofissure cordectomy	10
Lymph node removal	9
Pedicled flap	10
Free tissue flap	10
Local/regional flap	10
Pedicled pectoralis major myocutaneous flap (PMMF)	10