COST-EFFECTIVENESS ANLYSIS OF DOCETAXEL VERSUS STANDARD REGIMEN AS THE INDUCTION CHEMOTHERAPY OF LOCALLY ADVANCED HEAD AND NECK SQUAMOUS CELL CARCINOMA IN POLAND

Walczak J.[1], Nogas G.[1], Lasota K.[1], Malczak I.[1], Pawlik D.[1], Semeniuk A.[1], Simon A.[1], Bryl M.[1], Lis J.[2]

[1]Arcana Institute, Cracow, Poland, [2]Sanofi-Aventis, Warsaw, Poland

INTRODUCTION:

Head and neck squamous cell carcinomas (HNSCC) constitute 10% of all malignant cancers. 40% of HNSCC occur in the oral cavity, 25% in the larynx and 15% in the throat. The number of incidence in males is four times more frequent than in females. Generally HNSCC appears between the sixth and seventh decade of life [1].

Head and neck squamous cell carcinoma has an estimated annual global incidence of about 600,000 cases [2]. In Poland, about 5,700 new cases and 3,600 of deaths are stated annually [1].

Induction therapy involves the use of chemotherapy before patients receive chemoradiotherapy (CRT) or radiotherapy (RT) with the aim of shrinking tumors and reducing the risk of distant metastases development [3].

OBJECTIVES:

The aim of the analysis was to estimate the cost-effectiveness of docetaxel plus cisplastin and 5-fluorouracil (TPF) vs. standard regimen cisplastin and 5-fluorouracil (PF) as an induction chemotherapy followed by concurrent radiation (RCT TAX 323 [5]) or chemoradiation therapy (RCT TAX 324 [6]) in locally advanced unresectable head and neck squamous cell carcinoma in Poland.

METHODS:

Two cost-effectiveness Markov models (based on randomized clinical trials TAX 324 or TAX 323) were constructed using *TreeAge Pro 2008*.

The cost-effectiveness analyses (CEA) were conducted from the payers' perspective (National Health Fund and patient), using clinical data from published sources and Polish expense data assuming a 15-year time horizon. In line with Polish guidelines, the costs and benefits were discounted at 5% annual rate. To estimate the robustness of results, one-way and two-way sensitivity analyses were performed.

The target population were adult patients with locally advanced (stages III or IV) HNSCC that had been diagnosed by histologic or cytologic analysis.

The unit of effectiveness in the analysis was 'life years gained' (LYG). The outcome of the analysis was an incremental cost-effectiveness ratio (ICER), which presents the cost of gaining one additional life year (LYG) in the case of use the chemotherapy with docetaxel instead of standard regimen.

Based on a systematic review two randomized clinical trials were included in the comparison: TAX 323 [4] and TAX 324 [5].

The following comparisons were considered:

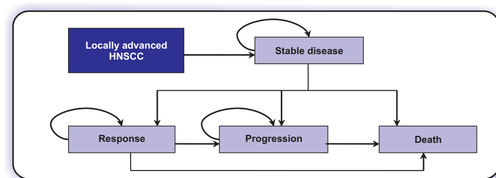
→ **TPF4** vs. **PF4** – The **TPF4** regimen consisted of docetaxel at a dose of 75 mg per square meter of body-surface area (BSA) administered as a 1-hour infusion on day 1, followed by cisplatin, at a dose of 75 mg per square meter of BSA, administered as a 1-hour infusion on day 1, and fluorouracil at a dose of 750 mg per square meter per day, administered by continuous infusion on days 1 to 5. The **PF4** regimen consisted of cisplatin at a dose of 100 mg per square meter of BSA, administered as a 1-hour infusion on day 1, followed by fluorouracil at a dose of 1000 mg per square meter per day, administered by continuous infusion on days 1 to 5. Treatment was administered every 3 weeks (defined as one cycle) for up to four cycles [4];

→ **TPF3** vs. **PF3** – The **TPF3** regimen consisted of docetaxel at a dose of 75 mg per square meter of BSA, administered as a 1-hour intravenous infusion, followed by intravenous cisplatin (100 mg per square meter), administered during a period of 0.5 to 3 hours, followed by fluorouracil (1000 mg per square meter per day) administered as a continuous 24-hour infusion for 4 days. Patients in the **PF3** group received intravenous cisplatin (100 mg per square meter), followed by fluorouracil (1000 mg per square meter per day) as a continuous 24-hour infusion for 5 days. Induction chemotherapy was given every 3 weeks (defined as one cycle) for three cycles [5].

It was assumed that mean BSA is 1,7 m^2.

The following states were considered in the model: "stable disease", "response", "progression" and "death".

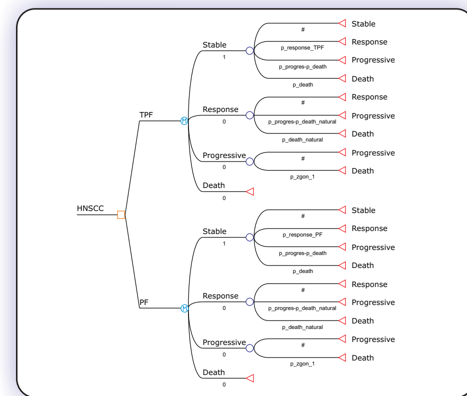
Figure 1.



In the Markov model, a cycle length of 3 weeks was used to coincide with the induction chemotherapy cycle length. The Markov model was constructed for a 15-year time horizon (260 cycles).

Transition probabilities were derived from the literature, including clinical trial reports and case series. Weibull distribution was used to estimate transition probabilities from "progression" state to "death" state and from "stable disease" state to "progression" state. Wherever data was missing, expert opinion was used.

Figure 2.



In the analysis, direct medical costs were considered using Polish cost data:

- costs of induction chemotherapy (drugs, hospitalization, premedication),
- costs of chemoradiotherapy or radiotherapy (drugs, hospitalization, premedication),
- costs of serious adverse events,
- costs of surgeries,
- costs of pain treatment,
- costs of palliative care in case of a relapse,
- costs of health state monitoring,
- cost of terminal care.

To calculate resource use data of Polish costs, Polish guidelines regarding HNSCC treatment, expert opinion and data from RCT studies were used.

Table 1.

Parameters	Chemotherapy regimens	
	TPF4	PF4
Chemotherapy costs (including hospitalization) [PLN]	6,519.68	1,804.47
Premedication costs [PLN]	133.70	104.42
Costs of serious adverse events treatment connected with chemotharapy [PLN]	4,478.77	5,329.08
Radiotherapy costs [PLN]	9,600.00	
Costs of serious adverse events treatment connected with radiotherapy [PLN]	1,342.32	1,295.91
Surgery costs [PLN]	9,240.00	
Costs of monitoring – 1st year after treatment finish [PLN]	45.97	45.94
Costs of monitoring – 2nd year after treatment finish [PLN]	32.17	32.14
Costs of monitoring – 3rd year after treatment finish [PLN]	27.57	27.54
Costs of monitoring – 4th year after treatment finish [PLN]	22.96	22.94
Costs of pain treatment after finishing the therapy [PLN]	34.19	34.19
Cost of enteral in progression state/cycle [PLN]	148.89	
Cost of stomach tube [PLN]	70.42	
Cost of tracheotomy [PLN]	1,560.00	
Cost of gastrostomy [PLN]	2,580.00	
Costs of pain treatment in patients with progressive disease [PLN]	133.63	125.15
Costs of second line chemotherapy [PLN]	22.61	
Costs of terminal care [PLN]	817.11	

1€ = 4.55 PLN; 25.03.2009

Table 2.

Parameters	Chemotherapy regimens	
	TPF3	PF3
Chemotherapy costs (including hospitalization) [PLN]	6,495.56	1,771.30
Premedication costs [PLN]	133.70	104.42
Costs of serious adverse events treatment connected with chemotharapy [PLN]	5,935.66	5,421.43
Costs of chemoradiotherapy (including hospitalization and premedication) [PLN]	8,194.42	
Costs of serious adverse events treatment connected with chemoradiotherapy [PLN]	2,717.81	2,933.29
Surgery costs [PLN]	9,240.00	
Costs of monitoring – 1st year after treatment finish [PLN]	46.59	46.18
Costs of monitoring – 2nd year after treatment finish [PLN]	32.79	32.37
Costs of monitoring – 3rd year after treatment finish [PLN]	28.19	27.77
Costs of monitoring – 4th and 5th year after treatment finish [PLN]	23.59	23.17
Costs of pain treatment after finishing the therapy [PLN]	34.19	
Cost of enteral in progression state/cycle [PLN]	148.89	
Cost of stomach tube [PLN]	70.42	
Cost of tracheotomy [PLN]	1,560.00	
Cost of gastrostomy [PLN]	2,580.00	
Costs of pain treatment in patients with progressive disease [PLN]	136.50	135.85
Costs of second line chemotherapy [PLN]	22.61	
Costs of terminal care [PLN]	817.11	

1€ = 4.55 PLN; 25.03.2009

RESULTS:

Average costs of the treatment for HNSCC (including chemotherapy, radiation or chemoradiation therapy, treatment of serious adverse events, surgery, health state monitoring, relapse treatment and palliative care) were: 54,708 PLN for TPF3 and 40,614 PLN for PF3 basing on TAX 324 and 46,107 PLN for TPF4 and 27,510 PLN for PF4 basing on TAX 323.

Based on TAX 324 treatment effects (per patient) were 4.3631 LYG vs. 3.4183 LYG respectively for TPF3 and PF3 regimens. Based on TAX 323 treatment effects (per patient) were 1.9694 LYG for TPF4 vs. 1.6875 LYG for PF4.

ICER for the TPF3 vs. PF3 comparison for trial TAX 324 was 14,916.40 PLN/LYG and 65,958.51 PLN/LYG for the TPF4 vs. PF4 comparison for trial TAX 323.

Regarding Polish willingness to pay (WTP) thresholds, the regimen TPF3 is highly cost-effective and the regimen TPF4 is cost-effective.

Figure 3.
Cost-Effectiveness Analysis at HNSCC TPF3 vs PF3

Figure 4.
Cost-Effectiveness Analysis at HNSCC TPF4 vs PF4

The robustness of the models was tested in the sensitivity analyses which proved stability of the results.

CONCLUSIONS:

The docetaxel regimens are more effective and more expensive in the induction treatment of patients with locally advanced unresectable HNSCC, compared with PF chemotherapy. ICERs are below the acceptable threshold; therefore the docetaxel therapies (TPF3 and TPF4) can be considered a cost-effective treatment for locally advanced unresectable HNSCC in Poland.

REFERENCES:

1. Gliński P. B., Ząbek M., Urbański J. *Podstawowe zasady postępowania z chorymi na raka płaskonabłonkowego głowy i szyi*, Współczesna Onkologia 2006; 10 (6): 263–267
2. Bourhis J., Le Maitre A., Baujat B. *Individual patients data meta-analyses in head and neck cancer*, Current Opinion in Oncology 2007; 19: 188–194
3. Final Appraisal Report. Docetaxel for locally advanced squamous cell carcinoma of the head and neck; Advice No: 1008; All Wales Medicines Strategy Group
4. Vermorken J. B., Remenar E., van Herpen C., Gorlia T. Cisplatin, *Fluorouracil, and docetaxel in unresectable head and neck cancer*. The New England journal of medicine 2007; 357(17): 1695–704
5. Posner M. R., Hershock D. M., Blajman C. R., Mickiewicz E. *Cisplatin and fluorouracil alone or with docetaxel in head and neck cancer*. The New England journal of medicine; 2007; 357 (17): 1705–15

This analysis was supported by Sanofi-Aventis

Arcana Institute ul. St. Dąbka 8, 30-732 Cracow, Poland, tel./fax. +48122636213, e-mail: kontakt@inar.pl www.inar.pl