

**REPORT ASCO 2001 SAN FRANCISCO : LUNG CANCER**  
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In a recent paper in the Journal of Clinical Oncology (19:1734; 2001), the North-American randomised studies from the recent decades dealing with advanced non-small cell lung (NSCLC) cancer were reviewed. One important conclusion was that most of these studies were underpowered to examine possible survival benefits of one therapy versus another. In the time-period 1973-1983, only 77 patients on average per arm were included. This increased to 121 patients per arm, in the period ranging from 1984 till 1994. Another notable conclusion was that only 5 of the 33 studies reviewed demonstrated a median survival benefit of at least 2 months when the “new arm” was compared to the standard treatment.

Nonetheless, based on historical comparison and meta-analyses, most colleagues now agree that chemotherapy has a role in advanced NSCLC, and that a moderate progress has been made with the new drugs such as gemcitabine, vinorelbine and the taxanes. From historical data, it can be said that advanced NSCLC treated with best supportive care alone has a median survival of 20 weeks, and a one-year survival rate of 10%. When treated with cisplatin + an older drug, the “25-rule” applies: a 25% response rate, a 25 weeks median survival time, and a 25% one-year survival rate. When treated with cisplatin + a new drug, we have reached the “33-rule”: 33% response rate, 33 weeks median survival, and 33% one-year survival rate. This is of course a schematic and easy-to-remember statement, but it is very representative for most large-scale modern studies.

The lung session of the 2001 ASCO meeting was characterised by several interesting, mainly European, trials that had sufficient power and number to yield some interesting conclusions. Four of these large trials will be discussed here:

- an Italian trial (abstr. 1227) on 612 patients, comparing cisplatin-vinorelbine (local reference) to either cisplatin-gemcitabine or carboplatin-paclitaxel,
- an EORTC trial (abstr. 1228) on 480 patients, comparing cisplatin-paclitaxel (local reference) to cisplatin-gemcitabine or gemcitabine-paclitaxel,
- a Spanish trial (abstr. 1229) on 562 patients, comparing cisplatin-gemcitabine (local reference) to a triplet (cisplatin-gemcitabine-vinorelbine) or a sequential platinum-free regimen (gemcitabine-ifosfamide-vinorelbine),
- an International trial (abstr. 1252) on 1220 patients, comparing cisplatin-vinorelbine (local reference) to cisplatin-docetaxel or carboplatin-docetaxel.

The reported efficacy results of these trials are listed in table 1. Pairwise comparison of different treatment arms within these studies yields a lot of information relevant to different questions on the optimal treatment of **advanced** NSCLC, as discussed by Alan Sandler at the meeting:

**1. Which new drug is preferably added to platinum?**

According to the Italian and EORTC study, there was no real difference between gemcitabine, vinorelbine or paclitaxel. According to the International study, docetaxel was slightly superior to vinorelbine when added to cisplatin (P=0.04). In terms of toxicity, it was reported that vinorelbine was characterised by clearly more neutropenia, while paclitaxel is characterised by more neurotoxicity.

**2. Which platinum component is to be preferred?**

The International trial contains the largest evidence ever presented regarding this question. Although the study was designed to compare the two docetaxel arms to cisplatin-vinorelbine, the difference between treatment with docetaxel with either cisplatin or carboplatin is striking: the cisplatin-arm was nearly 2 months superior in median survival, and 10% superior in one-year survival. No significance was reported, since this comparison was not planned according to the study design, but obviously, this is an important finding.

**3. Do we need a platinum component?**

The EORTC and Spanish trial contain information on this very actual question. In both studies, the platinum-free arm was inferior in terms of response and survival, reaching a nearly significant level in the EORTC experience. Certainly more and different data are needed before the 20 years of experience with platinum-based therapy can be safely abandoned.

#### **4. Is three drugs better than two?**

According to the Spanish trial, this was clearly not the case. Cisplatin-gemcitabine was identical to cisplatin-gemcitabine-vinorelbine in terms of efficacy (both response and survival), while there a substantial increase in toxicity (and cost of course) in the triplet arm. Again more and different data are needed to change this point of view.

#### **5. Should performance status and age influence our choice of treatment?**

Age per se should not, on the condition of a good performance status (Karnofsky  $\geq 80\%$ ). In case of poor performance status, platinum-based therapy should be avoided.

Interesting information on possible treatment alternatives in these elderly or less fit patients was brought in another Italian study (abstr. 1230, table 2). According to this experience in 700 patients, combination therapy of gemcitabine plus vinorelbine did not yield better efficacy in terms of response or median survival than single agent gemcitabine or single agent vinorelbine. Furthermore, there was no difference in quality-of-life between the three arms. Neutropenia was most prominent in the vinorelbine arm.

In summary, a duplet therapy containing platinum, preferably cisplatin, plus one of the new drugs remains the standard treatment in **advanced** NSCLC patients with a good performance status. There are not enough data to consider non-platinum regimens or triplet regimens in standard clinical practice, some data even suggest the opposite. In elderly or unfit patients, single agent treatment with one of the milder new agents is a fairly reasonable choice.

Table 1

	cis-gem	cis-vino	cis-pacl	cis-doce	cis-gem-vino	car-pacl	car-doce	gem-pacl	gem-vino-ifo	P-value
<b>Response rate (%)</b>										
Italian trial (612 pts)	30	30				32				NS
Eortc trial (480 pts)	36		31					27		0.30
Spanish trial (562 pts)	43				38				26	NS
International (1220 pts)		NR		NR			NR			-
<b>Median survival (mo)</b>										
Italian trial (612 pts)	9.8	9.5				9.9				NS
Eortc trial (480 pts)	8.8		8.1					6.9		<b>0.09</b>
Spanish trial (562 pts)	8.7				7.9				8.1	NS
International (1220 pts)		10		10.9			9.1			<b>0.04</b>
<b>1-year survival (%)</b>										
Italian trial (612 pts)	NR	NR				NR				-
Eortc trial (480 pts)	32		35					26		<b>0.09</b>
Spanish trial (562 pts)	34				31				35	NS
International (1220 pts)		42		47			38			<b>0.07</b>
<b>Mean number of cycles</b>										
Italian trial (612 pts)	4.1	3.2				4.2				-
Eortc trial (480 pts)	5		5					4		-
Spanish trial (562 pts)	4				4				4	-
International (1220 pts)		4		5			6			-

Table 2

	gem	vino	gem-vino	P-value
Response rate (%)	17	18	20	NS
Median survival (mo)	7	8	8	NS
1-year survival (%)	26%	41%	31%	NS