Preoperative concurrent chemoradiotherapy in non-small-cell lung cancer. Feasibility, toxicity and long-term results of a phase II study

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ABSTRACT

Background: *Multimodality treatment are employed to improve prognosis of resecable non-small cell lung cancer. The risks and benefits of radiochemotherapy either on surgical morbility and mortality or in improving treatment outcome are still in debate. We carried out a phase II trial to evaluate the feasibility, toxicity and effect on survival of polychemotherapy delivered concurrently with accelerated modified hyperfracctionated radiotherapy in non-small cell lung cancer stage III patients.*

Methods: *38 patients with locally advanced stage III non-small cell lung cancer received neoadjuvant therapy consisting of accelerated modified hyperfracctionated radiotherapy 40,2 Gy in 15 days with a second cycle of chemotherapy using cisplatin 80 mg/m² on day 1, ifosfamide 1,5 gr/m² on day 1, and etoposide 100 mg/m² for 3 days and mesna every 21 days. Patients after surgery received 2 cycles of chemotherapy.*

Results: *From Octobre 1997 to Octobre 2001, 38 patients were entered into the study. The most frequent cell type was squamous cell carcinoma (20 patients-52,6%-) and adenocarcinoma (12 patients-31,6%-). Performance status was 0 in 3 patients (8%), 1 in 31 (81,5%) and 2 in 4 (10,5%). The prominent grade 3-4 hematolological side effect was: neutropenia in 9 patients (29,1%), trombocytopenia in 5 (15,7%), anemia in 4 (13%). The grade 3-4 non-hematological side effects was: esophagitis in 9 patients (29%) and emesis in 2 (7%) . The response rate was 45% (CR 1 and PR 16), stable disease in 34% and progression disease in 21%. Surgical-pathological staining showed downstaging in 20 patients including complete sterilization of the tumor in 13 patients (34%). The median survival for all 38 patients was 21,85 months with 21,4% 5-years survivors.*

Conclusions: *this multimodality approach to satge III NSCLC has a tolerable toxicity profile and encouraging survival.*

1. BACKGROUND

- Multimodality treatment are employed to improve prognosis of resecable non-small cell lung cancer. The risks and benefits of radiochemotherapy either on surgical morbility and mortality or in improving treatment outcome are still in debate.

- This phase II was designed to assess the feasibility, toxicity and efficacy of concurrent chemoradiotherapy.

2. ENDPOINTS

- **Primary endpoints**:
  - Response rate.
  - Toxicity.
- **Secondary endpoints**:
  - Time to progression.
  - Survival.

3. ELEGIBILITY CRITERIA

- Age < 75 years
- Resectable IIIA/IIIB NSCLC
- PS 0 - 2.
- Weight loss <10%.
- One measurable disease.
- Normal vital functions.
- Predicted post-operative Forced Expiratory Volume (ppo FEV1) > 40%

4. PATIENTS FEATURES

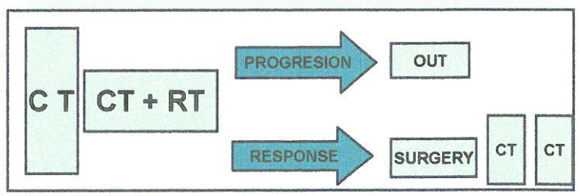
38 patients were included from October 1997 to October 2001.

- Median age (range): 64 years (39-77)
- Male/female: 32/6
- PS 0/1/2: 3/31/4
- Cell type tumors: squamous cell carcinoma 20 (52,6%), adenocarcinoma 12 (31,6%), large cell carcinoma 5 (13,2%), NSCLC 1(2,6%)
- Stage: IIIA 36/ IIIB 2
- Assessable to response: 38 pts.
- Evaluable for survival: 38 pts.

5. TREATMENT SCHEDULE

- **CT**: cisplatin 80 mg/m² on day 1, ifosfamide 1,5 gr/m² on day 1, etoposide 100 mg/m² for 3 days , and mesna every 21 days.

- **RT**: modified hiperfractionated accelerated RT with concomitant boost, 1,8Gy + 0,88Gy x 15 days, total dose 40,2 Gy.



6. TOXICITY

Major acute toxicities (Grade III or IV) were:

- Esophagitis: 9 pts (29%).
- Emesis: 2 pt (6,9%).
- Neutropenia: 9 pts (29,%).
- Anemia: 4 pt (13%).
- Trombocytopenia: 5 pt (15,7%).

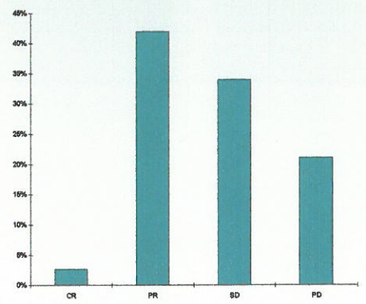
There was no treatment related death.

7. EFFICACY

38 patients were assessable for response.

- Complete response: 1 pts (2,6%).
- Partial response: 16 pts (42,1%).
- Stable disease: 13 pts (34,2%).
- Progresion disease: 8 pts (21,1%).

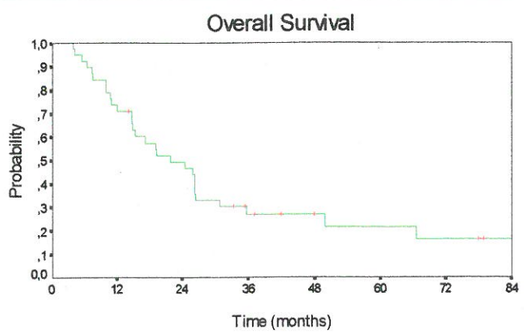
Resectable patients: 29/38 (76%)

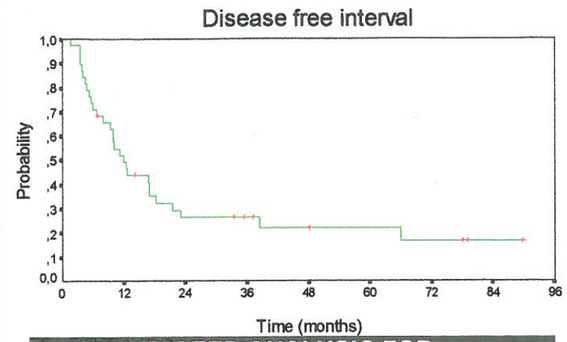


- Relapses: 21/30 (70%).
  - -local relapse: 11/21 (52%)
  - -metastatic relapse 10/21 (48%)
  - -8 relapses in SNC

8. TIME TO PROGRESION / SURVIVAL

- Median TTP was 11,91 m
- Median survival was 21,85 m





9. UNIVARIATED ANALYSIS FOR SURVIVAL

	5y OS	p
Pneumonectomy **Lobectomy**	33,3% 25,4%	0.003
pT0 **pT1-4**	35% 22,2%	0.001
pN0 **pN1-2**	35,5% 18,2%	0.0009
Downstaging **Yes** **No**	31,8% 22,2%	0.0013

10. CONCLUSIONS

- This multimodality approach to stage III NSCLC has a tolerable toxicity profile and encouraging survival.

- Pathologic downstaging is an important predictor of improved survival.