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| Table S1. Induction chemotherapy followed by chemoradiation versus chemoradiation alone in LASCCHN |

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|   | **Hitt et al., Annals of Oncology 2014 [15]** | **Cohen et al., JCO 2014 [16]** | **Haddad et al., Lancet Oncology 2013 [17]** |
| **Toxicity grading scale** | **NCI-CTCAE** **version 2.0** | **NCI-CTCAE** **version 3.0** | **NCI-CTCAE** **version 3.0** |
|  | **Grade 3-4 toxicities during the induction period with TPF 1** | **Grade 3-4 toxic effects during the whole treatment** |
| **Neutropenia** | 19% | 11% |  | **TPF 4 --> CRT 5** | **CRT 6** |
| **Febrile neutropenia** | 17% | NA | **Mucositis** | 47% | 16% |
| **Asthenia/Fatigue** | 10.5% | 7.4% | **Febrile neutropenia** | 23% | 1% |
| **Decreased appetite/Anorexia** | 5.2% | 7.4% | **Pain** | 3% | 12% |
| **Vomiting** | 6.6% | 2.2% | **Xerostomia** | 7% | 7% |
| **Dysphagia** | 1.3% | 2.9% | **Neuropathy** | 0% | 3% |
| **Stomatitis/mucositis**  | 9.1% | 9.00% | **PEG tube**  | 79% | 85% |
| **Diarrhea** | 7.2% | 5.1% |  |  |  |
| **Infection** | 4.6% | 2.9% |  |  |  |
| **Nephropathy/Creatinine** | 6.5% | 0.7% |  |  |  |
| **Ototoxicity** | 0.7% | NA |  |  |  |
| **Neurotoxicity** | 0% | NA |  |  |  |
| **Others** | 26.2% | NA |  |  |  |
|  | **Toxicities grade 3-4 during CRT** |  |  |  |
|  | **TPF --> CRT 2** | **CRT 2** | **TPF --> CRT 3** | **CRT 3** |  |  |  |
| **Neutropenia** | 30.2% | 20.4% | 3.2% | 1.5% |  |  |  |
| **Febrile neutropenia** | 4.7% | 0,90% | NA | NA |  |  |  |
| **Asthenia** | 6.6% | 3.4% | 4.8% | 3% |  |  |  |
| **Decreased appetite/Anorexia** | 1.9% | 1.7% | 11% | 14% |  |  |  |
| **Vomiting** | 4.7% | 8,50% | 3.2% | 2.3% |  |  |  |
| **Dysphagia** | 8.5% | 4.2% | 12% | 15% |  |  |  |
| **Odynophagia** | 13.2% | 6.8% | NA | NA |  |  |  |
| **Stomatitis/mucositis**  | 49% | 33% | 49% | 44.5% |  |  |  |
| **Diarrhea** | 0% | 0,90% | 0% | 3% |  |  |  |
| **Infection** | 4.7% | 4.3% | 11% | 14% |  |  |  |
| **Rash/Dermatitis** | 4.7% | 7.6% | 18% | 24% |  |  |  |
| **Nephropathy/Creatinine** | 1.9% | 5.1% | NA | NA |  |  |  |
| **Ototoxicity** | 0.9% | 0.9% | NA | NA |  |  |  |
| **Neurotoxicity** | 0.9% | 1.7% | NA | NA |  |  |  |
| **Others** | 27% | 31.7% | NA | NA |  |  |  |
| Abbreviations: JCO: Journal of Clinical Oncology; NCI-CTC AE: National Cancer Institute-Common Toxicity Criteria for Adverse Events; PEG tube: percutaneous endoscopic gastrostomy; CRT: chemoradiation |  |  |
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| 1. TPF: docetaxel (day 1, 75mg/m2), cisplatin (day 1, 75mg/m2 ) and 5-fluorouracil (day 1-5, 750 mg/m2/day). |  |  |  |
| 2. CRT: Radiotherapy, conventional fractionation, total dose of 70 Gy in 35 fractions and cisplatin 100mg/m2 on days 1, 22 and 43. |  |  |  |
| 3. CRT: Radiotherapy - 3D-conformal or intensity-modulated radiation therapy, total dose of 74-75 Gy, given as fractions of 0,15 Gy twice daily every other week and docetaxel, 5-fluorouracil and hydroxyurea. |  |  |  |
| 4. TPF: docetaxel (day 1, 75mg/m2), cisplatin (day 1, 100mg/m2 ) and 5-fluorouracil (day 1-4, 1000 mg/m2/day). |  |  |  |
| 5. CRT: poor responders: radiotherapy, accelerated concomitant boost over six weeks, total of 72 Gy in 1,8/1,5 Gy fractions and weekly docetaxel (20 mg/m2) for four weeks; favourable reponders: radiotherapy, coventional fractionation, total 70 Gy in 35 fractions with weekly carboplatin (AUC=1.5) for seven weeks. |  |  |  |
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| 6. CRT: radiotherapy, accelerated concomitant boost over seven weeks, total of 72 Gy in 1.8/1.5 Gy fractions and cisplatin 100 mg/m2 on days 1 and 22. |  |  |  |
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| Table S2. Induction chemotherapy for larynx preservation |
|   | **Pointreau, JNCI 2009 [31]** |
| **Toxicity grading scale** | **NCI-CTC version 2.0 during IC and RTOG scoring system for acute and late RT toxic effects** |
|  | **Acute toxicity of chemotherapy** |
|  | **TPF 1** | **PF 2** |
| **Death due to toxicity** | 2.7% | 1.9% |
| **Alopecia grade 2** | 19.4% | 2% |
| **Neutropenia grade 4** | 31.5% | 17.6% |
| **Febrile neutropenia** | 10.9% | 5.8% |
| **Thrombocytopenia grade 3-4** | 1.8% | 7.8% |
| **Creatinine elevation grade 4** | 0.00% | 2% |
| **Nausea/vomiting grade 1-3** | 44.4% | 44.1% |
| **Stomatitis grade 3-4** | 4.6% | 7.8% |
|  | **Late toxicity** |
| **Larynx toxicity grade 4** | 6.2% (2 patients treated with CRT) | 13.6% (3 patients treated with CRT) |
| **Mucous membrane grade 3-4** | 1.00% | 0% |
| **Salivary glands** | 6.10% | 2.2% |
| **Subcutaneous tissue** | 4% | 6.6% |
| Abbreviations: JNCI: The Journal of the National Cancer Institute; NCI-CTC: National Cancer Institute-Common Toxicity Criteria; IC: induction chemotherapy; RTOG: Radiation Therapy Oncology Group; RT: radiotherapy; CRT: chemoradiation. |
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| 1. TPF: 3 cycles of docetaxel (75 mg/m2 day 1), cisplatin (75 mg/m2 day 1) and 5-fluorouracil (750 mg/m2 day 1-day 5), 1x/3 weeks |
| 2. PF: 3 cycles of cisplatin (100 mg/m2 day 1) and 5-fluorouracil (1000 mg/m2 day1-day5), 1x/3weeks |