*consolidation phase can be used in the neo-adjuvant setting prior to chemoradiation

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| **Indication** | Patients with stage IIIA/IIIB non-small cell lung cancer. |
| **Treatment Intent** | Radical<br><br>Neoadjuvant prior to chemoradiation (use the consolidation phase of this protocol) |
| **Frequency and number of cycles** | Repeat every 7 days for 6 cycles concurrent with radiotherapy.<br><br>Consolidation doses on day 64 and 85 (see details below). |
| **Monitoring Parameters pre-treatment** | • **Virology screening:** All new patients referred for systemic anti-cancer treatment should be screened for hepatitis B and C and the result reviewed prior to the start of treatment. Patients not previously tested who are starting a new line of treatment, should also be screened for hepatitis B and C. Further virology screening will be performed following individual risk assessment and clinician discretion.<br>• EDTA or estimated CrCl using C+G should be used to measure GFR prior to cycle 1. Must be >/=30ml/min. Repeat EDTA if creatinine clearance drops by 25%. For subsequent weekly doses during concurrent therapy, a >10% change in the serum creatinine, will warrant a recalculation of the carboplatin dose.<br>• Monitor FBC, U&E and LFT each cycle.<br>• **For Concurrent therapy**: If neuts <1 or PLT <100 d/w consultant, consider delaying D1 by 1 week. If neuts >/= 1 and PLT >/= 100 continue with treatment.<br>• **For Consolidation therapy**: If neuts <1.5 or PLT <100 d/w consultant, consider delaying D1 by 1 week. If neuts >/= 1.5 and PLT>/= 100 continue with treatment.<br>• GCSF should be considered during concurrent therapy if more than one delay and/or before dose reduction, or if during preceding cycle, the patient has experienced neuts <0.5 or has had febrile neutropenia.<br>• **Hepatic impairment:**<br>o Carboplatin: No dose adjustment required.<br>o Paclitaxel: If bilirubin < 1.25 x ULN and transaminase < 10 x ULN, dose at full dose. Otherwise consider dose reduction, not recommended in severe hepatic impairment.<br>• **Renal impairment:**<br>o Carboplatin: stop if CrCl <30ml/min.<br>o Paclitaxel: no dose reduction necessary.<br>• **Infusion related reactions:**<br>• **Paclitaxel:** Patients developing hypersensitivity reactions to Paclitaxel may be re-challenged with full dose Paclitaxel following prophylactic medication (e.g. famotidine 40mg po given 4 hours prior to treatment plus Hydrocortisone 100mg iv and chlorphenamine 10mg iv 30 minutes prior to treatment), then give paclitaxel over 3-6 hours (i.e. starting at over 6 hours and gradually increase rate if possible).<br>• To begin consolidation, all previous toxicities including neuropathy must have resolved to < grade 2.<br>• **Carboplatin:** Mild/moderate reactions (grade 1-2): If symptoms resolve after treatment with hydrocortisone and chlorphenamine, the infusion may be restarted at 50% rate for 30 mins, then, if no further reaction, increase to 100% rate.<br>If symptoms do not resolve after treatment with hydrocortisone and chlorphenamine, do not restart the infusion. At consultant's discretion, patients may be rechallenged at a later date with additional prophylaxis. In the event of further reaction (grade 1-3), stop infusion and consider alternative treatment.<br>Severe (grade 3): Do not restart infusion. Consider alternative treatment. |

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| | Anaphylaxis (grade 4): Follow anaphylaxis protocol. Discontinue permanently and consider alternative treatment.<br>• **Dose Reductions:**<br>• For concurrent therapy, paclitaxel and carboplatin will not be reduced.<br>• During consolidation if dose reduction is required, dose reduce paclitaxel to 150mg/m² and carboplatin to AUC 4.5.<br>• In the event of >/= grade 2 neuropathy reduce Paclitaxel to 150mg/m² and consider delay until recovery to </= grade 1.<br>• Stop paclitaxel in the event of recurrent >/= grade 3 neuropathy OR recurrent or persistent >/= grade 2 neuropathy following dose reduction<br>• Dose reduction should be considered if any other grade 3 or 4 non-haematological toxicity or repeat appearance of grade 2 (except N&V and alopecia). Delay until resolution of toxicity to </= grade 1<br>• **Drug interactions: (for comprehensive list refer to SPC/BNF)**<br>o **Paclitaxel**<br>Caution should be exercised when administering paclitaxel concomitantly with medicines known to inhibit either CYP2C8 or CYP3A4 (e.g. ketoconazole, erythromycin, fluoxetine, clopidogrel, cimetidine, ritonavir and nelfinavir); toxicity may be increased. CYP2C8 or CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, efavirenz, nevirapine) may reduce efficacy.<br>o **Carboplatin**<br>Caution with other nephrotoxic drugs. |
| **References** | KMCC protocol LUN-040 V2 LUNG NOG 27.06.2023 |

NB For funding information, refer to CDF and NICE Drugs Funding List

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**Concurrent: with radiotherapy**

**Repeat every 7 days for 6 cycles.**

| Day | Drug | Dose | Route | Infusion Duration | Administration |
|---|---|---|---|---|---|
| Day 1 | Dexamethasone | 8mg (may be reduced to 4mg in subsequent cycles) | IV | bolus | |
| | Chlorphenamine | 10mg | IV | bolus | Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion |
| | Ondansetron | <75yrs 16mg >/=75yrs 8mg | IV | 15 min | Sodium chloride 0.9% 50ml |
| | **Please ensure pre-meds are given 30 mins prior to paclitaxel** | | | | |
| | **PACLITAXEL** | **45mg/m²** | IV | 1 hour | In 250ml Sodium Chloride 0.9% (non-PVC bag and non-PVC giving set) via in-line 0.22 microns filter. Doses <75mg in 100ml sodium chloride 0.9% |
| | **CARBOPLATIN** | **AUC=2 Dose = Target AUC x (25 + GFR) (maximum dose=300mg)** | IV | 30 minutes | In 250-500ml glucose 5% |
| TTO | Drug | Dose | Route | Directions | |
| Day 1 | Dexamethasone | 4mg | PO | OM 2 days. Take with or just after food, or a meal | |
| | Metoclopramide | 10mg | PO | 10mg TDS for 3 days then 10mg up to 3 times a day when required (Maximum of 30mg per day). Do not take for more than 5 days continuously. | |

*consolidation phase can be used in the neo-adjuvant setting prior to chemoradiation

**Consolidation**: **First cycle to be given 28 days after last dose of concurrent chemotherapy**.
**Repeat every 21 days for 2 cycles**

| Day | Drug | Dose | Route | Infusion Duration | Administration |
|---|---|---|---|---|---|
| 1 | Dexamethasone | 16mg | IV | bolus | |
| | Chlorphenamine | 10mg | IV | bolus | Over 3 min through a fast running Sodium chloride 0.9% intravenous infusion |
| | Ondansetron | <75yrs 16mg >/=75yrs 8mg | IV | 15 minutes | Sodium chloride 0.9% 50ml |
| | **Please ensure pre-meds are given 30 mins prior to paclitaxel** | | | | |
| | **PACLITAXEL** | **200mg/m²** | IV | 3 hours | Diluted in 500ml sodium chloride 0.9% (non-PVC bag and non-PVC giving set) via in-line 0.22micron filter.<br>Doses <150mg in 250ml 0.9% sodium chloride |
| | **CARBOPLATIN** | **AUC=6**<br>**Dose = AUC X (GFR + 25)**<br>**Max dose 700mg** | IV | 30 minutes | 500ml glucose 5% |

| TTO | Drug | Dose | Route | Directions |
|---|---|---|---|---|
| Day 1 | Dexamethasone | 6mg | PO | OM for 3 days<br>Take with or just after food, or a meal. |
| | Metoclopramide | 10mg | PO | 10mg TDS for 3 days then 10mg up to 3 times a day when required (Maximum of 30mg per day).<br>Do not take for more than 5 days continuously. |
| | Filgrastim | 5mcg/kg | SC | OD<br>Starting on day 3 for 5 days. |