**Table S2:** Dose reduction criteria

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| --- | --- | --- |
| **Cardiac toxicity criteria** | | |
| CHF severe | Withdrawal | |
|
| CHF moderately symptomatic or  Asymptomatic | LVEF < 45%: withdrawal | |
| LVEF decrease 10-20 points and LVEF ≥45%: keep treatment | |
| LVEF decrease > 20 points : withdrawal | |
| **Hematology toxicity criteria** | | |
| **PLD+CPM** | | |
| 0.5x109 /l ≥ *N* < 1.5x109 /l and/or  25x109/l ≥ Plat < 75x109/l | interrupted until *N* < 1.5x109 /l and  Plat < 75x109/l | No dose reduction |
| *N* < 0.5x109 /l and/or Plat < 75x109/l | Interrupted until *N* < 1.5x109 /l and  Plat < 75x109/l | Dose reduction of 15% for both drugs |
| If a patient needs more than 2 weeks to recover normal levels of neutrophils or platelets, PLD plus CO was   withdrawal and patient start PYX treatment or surgery was performed at investigator criteria | | |

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Paclitaxel** | | | | | | | | | | | |
| *N* < 1.0x109 /l and/or Plat < 75x109/l | | | Interrupted until *N* < 1.5x109 /l and  Plat < 75x109/l | | | | Recovery ≤ 1 week: no dose reduction | | | | |
| Recovery ≤ 2 week: rechallenge at a   20 % dose reduction | | | | |
| If a patient needs more than 2 weeks to recover normal levels , paclitaxel was withdrawal and surgery was performed | | | | | | | | | | | |
| **Non-hematology toxicity criteria** | | | | | | | | | | | |
| **PLD+CPM** | | | | | | **PTX** | | | | | |
| Hand foot syndrome (HFS) | | | | | | Adverse Events | | | | | |
| G1 | Treatment not  interrupted | | | No dose reduction | | G1 | | Treatment not   interrupted | | | |
| G2 | interrupted until  ≤ G1 | | | No dose reduction | | G2 | | Treatment not  interrupted | | | |
| G3 | interrupted until  ≤ G1 | | | 15% dose reduction | | G3 | | interrupted until   ≤ G1 | | | |
| G4 | interrupted until  ≤ G1 | | | 25% dose reduction | | G4 | | interrupted until  ≤ G1 | | | |
| If a patient needs more than 2 weeks to G1, withdrawal PLD+CP  treatment and start with PTX | | | | | | If a patient more than 2 weeks to recover to G2, withdrawal PTX  treatment and surgery performed | | | | | |
| Mucositis | | | | | | Hypersensitivity | | | | | |
| G1 | | Treatment not  interrupted | | | No dose reduction | Immediately discontinued the infusion and appropriate symptomatic treatment. Treatment was restarted a lower speed. If tolerated, the infusion may then be completed over the next hour to a total of 90' | | | | | |
| G2 | | interrupted until  ≤ G1 | | | No dose reduction |
| G3 | | interrupted until≤ G1 | | | 15% dose reduction | **PLD+CPM, paclitaxel** | | | | | |
| Bilirubin > 2x normal lab value | | | | | |
| G4 | | interrupted until≤ G1 | | | 25% dose reduction | Treatment interrupted | | | | recovery in 3  weeks to G1 | Treatment not  interrupted |
| If patient needs more than 2 weeks to G1, withdrawal PLD+CP  treatment and start with PTX | | | | | | no recovery in 3 weeks  to G1 | Interrupted treatment  and surgery performed |
| Anaphylactic reaction during infusion | | | | | | Creatinine clearance  40-156 ml/min | | | Normal dose | | |
| Immediately discontinued the infusion and appropriate  symptomatic treatment. Treatment was restarted at a lower  speed. If tolerated, the infusion may than be completed over  the next hour to a total of 90 ' | | | | | |
| Creatinine clearance  ≤ 40 ml/min | | | If ≤ 3 weeks to normal, no interrupted treatment | | |
| If ≥3 weeks to normal, interrupted treatment and surgery performed | | |

Abbreviations: CHF: Congestive Heart Failure, LVEF: Left ventricular ejection fraction, N: Neutrophils, Plat: Platelels, G: Grade, PLD: Pegylated liposomal doxorubicin, CPM: Cyclophosphamide, PTX: Paclitaxel,