Table S2: Dose reduction criteria

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		
$0.5x10^9$ /l ≥ *N* < $1.5x10^9$ /l and/or $25x10^9$/l ≥ Plat < $75x10^9$/l	interrupted until *N* < 1.5x109 /l and Plat < 75x109/l	No dose reduction
N < 0.5x109 /l and/or Plat < $75x10^9$/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		

<table>
<tr><th colspan="6">Paclitaxel</th></tr>
<tr><td colspan="2">N < 1.0x109 /l and/or Plat < 75x109/l</td><td colspan="2">Interrupted until N < 1.5x109 /l and Plat < 75x109/l</td><td colspan="2">Recovery ≤ 1 week: no dose reduction</td></tr>
<tr><td colspan="4"></td><td colspan="2">Recovery ≤ 2 week: rechallenge at a 20 % dose reduction</td></tr>
<tr><td colspan="6">If a patient needs more than 2 weeks to recover normal levels , paclitaxel was withdrawal and surgery was performed</td></tr>
<tr><th colspan="6">Non-hematology toxicity criteria</th></tr>
<tr><th colspan="3">PLD+CPM</th><th colspan="3">PTX</th></tr>
<tr><td colspan="3">Hand foot syndrome (HFS)</td><td colspan="3">Adverse Events</td></tr>
<tr><td>G1</td><td>Treatment not interrupted</td><td>No dose reduction</td><td>G1</td><td colspan="2">Treatment not interrupted</td></tr>
<tr><td>G2</td><td>interrupted until ≤ G1</td><td>No dose reduction</td><td>G2</td><td colspan="2">Treatment not interrupted</td></tr>
<tr><td>G3</td><td>interrupted until ≤ G1</td><td>15% dose reduction</td><td>G3</td><td colspan="2">interrupted until ≤ G1</td></tr>
<tr><td>G4</td><td>interrupted until ≤ G1</td><td>25% dose reduction</td><td>G4</td><td colspan="2">interrupted until ≤ G1</td></tr>
<tr><td colspan="3">If a patient needs more than 2 weeks to G1, withdrawal PLD+CP treatment and start with PTX</td><td colspan="3">If a patient more than 2 weeks to recover to G2, withdrawal PTX treatment and surgery performed</td></tr>
<tr><td colspan="3">Mucositis</td><td colspan="3">Hypersensitivity</td></tr>
</table>

<table>
<tr><td>G1</td><td>Treatment not interrupted</td><td>No dose reduction</td><td colspan="4" rowspan="2">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'</td></tr>
<tr><td>G2</td><td>interrupted until ≤ G1</td><td>No dose reduction</td></tr>
<tr><td>G3</td><td rowspan="2">interrupted until≤ G1</td><td rowspan="2">15% dose reduction</td><td colspan="4">PLD+CPM, paclitaxel</td></tr>
<tr><td rowspan="2">G4</td><td colspan="4">Bilirubin > 2x normal lab value</td></tr>
<tr><td>interrupted until≤ G1</td><td>25% dose reduction</td><td rowspan="2">Treatment interrupted</td><td>recovery in 3 weeks to G1</td><td>Treatment not interrupted</td></tr>
<tr><td colspan="3">If patient needs more than 2 weeks to G1, withdrawal PLD+CP treatment and start with PTX</td><td>no recovery in 3 weeks to G1</td><td>Interrupted treatment and surgery performed</td></tr>
<tr><td colspan="3">Anaphylactic reaction during infusion</td><td rowspan="2">Creatinine clearance 40-156 ml/min</td><td colspan="2" rowspan="2">Normal dose</td></tr>
<tr><td colspan="3" rowspan="3">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 '</td></tr>
<tr><td rowspan="2">Creatinine clearance ≤ 40 ml/min</td><td colspan="2">If ≤ 3 weeks to normal, no interrupted treatment</td></tr>
<tr><td colspan="2">If ≥3 weeks to normal, interrupted treatment and surgery performed</td></tr>
</table>

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