

Regional Chemotherapy for triple negative breast cancer improves eligibility for surgical removal

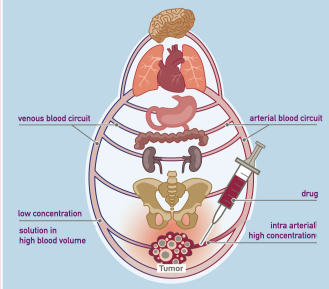
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Principle of Regional Chemotherapy

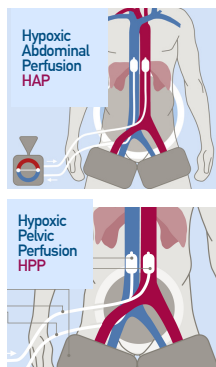
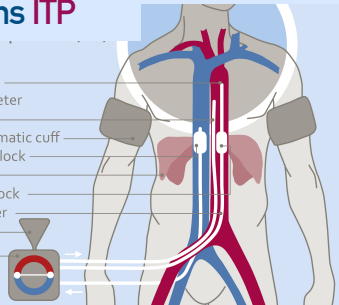


Background:

Multiple systemic treatment lines for triple negative breast cancer (TNBC) often lead to exhaustion and bone marrow suppression while response rates remain unsatisfactory. There is a need for new treatment options that increase the eligibility for surgical excision of primary tumors and metastases.

Isolated Thoracic Perfusions ITP

coaxial catheter
in stopflow catheter
angio catheter
upper arm pneumatic cuff
v. cava balloon block
diaphragm
aortic balloon block
stopflow catheter
cytotoxic drug
pump with chemofilter

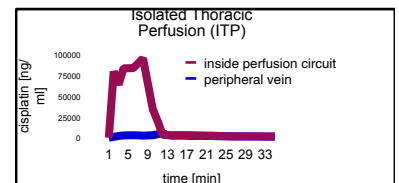


Material and Methods:

For isolated perfusion chemotherapy an isolated extracorporeal circuit that includes the tumor region was established with perfusion balloon catheters. Only low drug dosages were infused into the limited treatment volume. Isolated thoracic perfusion was performed for advanced primary tumors, lung metastases, and lymphatic or bone metastases in the thoracic region including the axilla. Trans-arterial chemoembolization was performed for liver metastases.

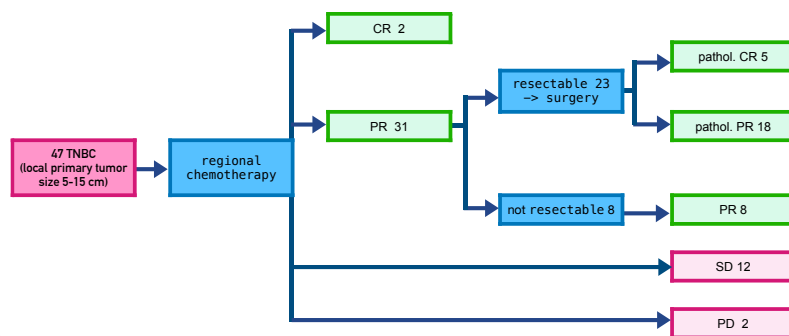
	Dosage Cisplatin [mg]	local cisplatin concentration [µg/ml]
ITP	80	95
HAP	50	60
HPP	50	380

peripheral cisplatin concentration:
< 5 µg/ml

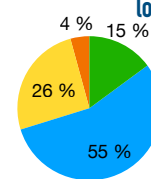


Chemofiltration: After the procedure and maximized drug uptake into the tumor cells a chemofiltration machine is connected and filtration up to 5 liter substitute volume is applied to avoid systemic drug exposure.

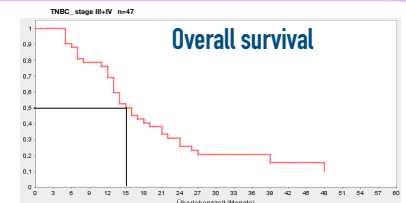
metastasized or recurrent TNBC FIGO III/IV



local response rates



● Complete Response
● Partial Response
● Stable Disease
● Progressive Disease



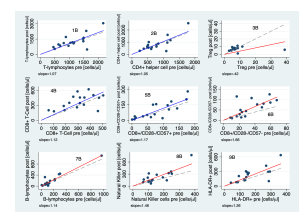
Immune response:

B-lymphocytes ↑ CD8+/CD28-/CD57- regulatory Tcells ↑

Natural Killer Cells ↑

Tregs ↓

HLA-DR+ cytotoxic Tcells ↑



Adverse events:

Adverse events:	n (%)
leukopenia grade >=2	1 (0.02%)
neuropathy	0 (0%)
lymph fistula	9 (19%) -> new technique now
wound infections	3 (6%) -> new technique now

Quality of Life:

Quality of Life:	n (%)
hair loss	5 (11%)
weakness	2 (4%)
pain	1 (2%)
EORTC (C30& BR45)	study still in progress

Results:

47 patients with metastasized or recurrent TNBC were treated with intra arterial infusion and isolated perfusion chemotherapy. Serum cisplatin levels at the tumor site reached up to 95 µg/ml with only limited total dosages of 50-90 mg cisplatin due to the reduced volume. The additional stopflow technique allowed for further increased drug concentration during the first five minutes and enhanced tissue drug uptake. The local response rate was 70% (33 pts). Median overall survival rate was 15 months.

Conclusions:

TNBC patients that suffer from unsatisfactory response or toxicity of systemic chemotherapy might benefit from isolated perfusions and intra arterial infusion techniques. Higher local drug concentrations and lower systemic concentrations increase the efficacy and decrease adverse events. A prospective clinical trial is planned to further evaluate regain of resectability.