



Individualized treatment for ovarian disease control using PIPAC as neo adjuvant treatment.

Pr Marc Pocard

INSERM U 965 : CART : Carcinomatosis angiogenesis and translational research

Oncological surgical unit = Lariboisière's Hospital, Paris, France



Individualized treatment for ovarian disease control using PIPAC as neo adjuvant treatment

Hypothesis:

Histological analysis of ovarian tumor, reveal more than 60 different histological aspects.

Primary peritoneal disease is probably the last form of ovarian cancer, underlining the major mixed situation encountered in clinical practice.

Advanced ovarian cancer, as majority of cancer is a heterogeneous process regarding genomic tumor process.

Different molecular profile

Microenvironment analysis is important

Individualized treatment for ovarian disease control using PIPAC as neo adjuvant treatment

Hypothesis:

Taking together, all that points enhance the necessity to propose for each patient a specific treatment process as for others cancers.



Contents lists available at [ScienceDirect](#)

Critical Reviews in Oncology/Hematology

journal homepage: www.elsevier.com/locate/critrevonc

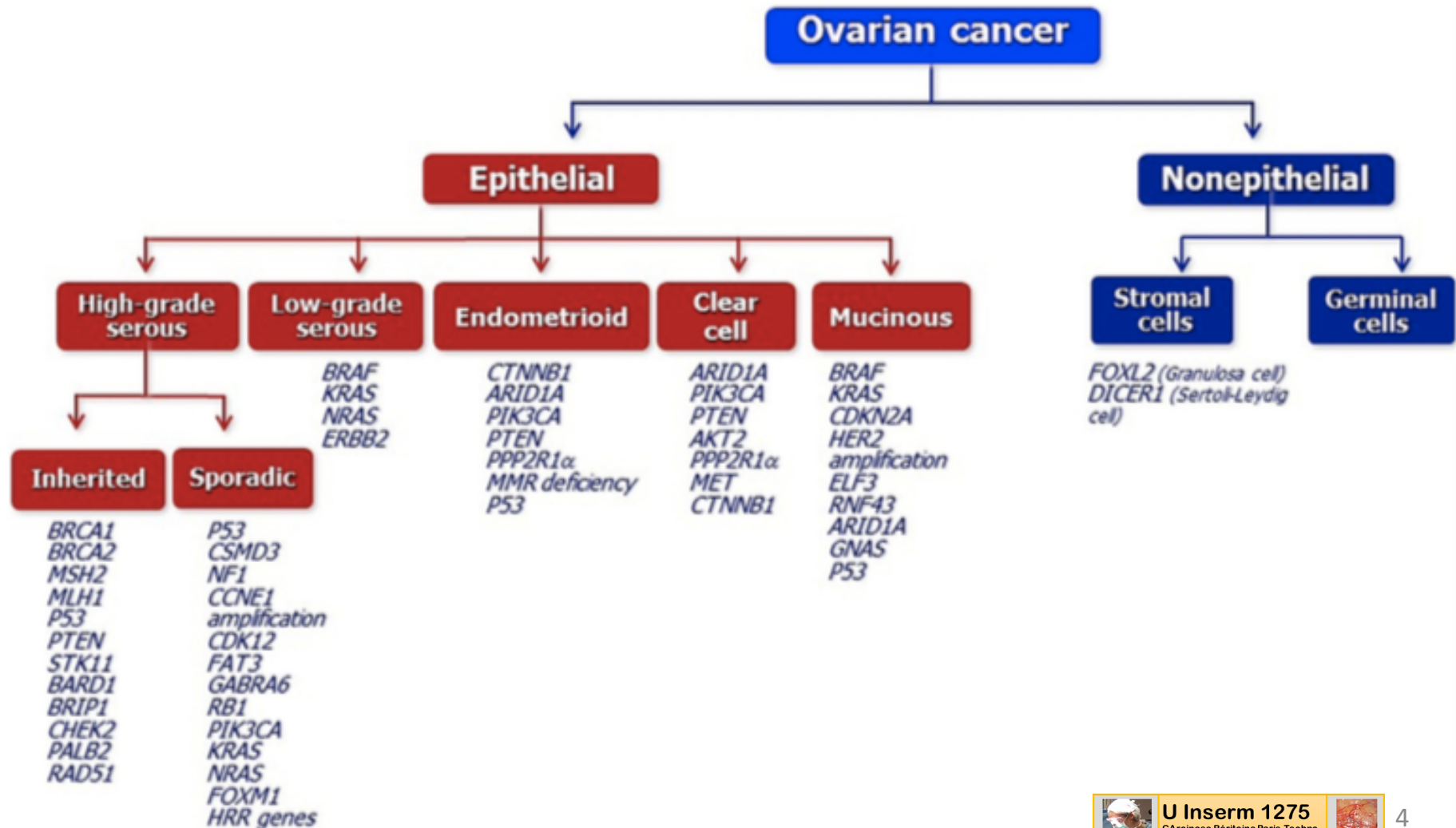
Ovarian cancer: Novel molecular aspects for clinical assessment

Raffaele Palmirotta, Erica Silvestris, Stella D'Oronzo, Angela Cardascia, Franco Silvestris*

Department of Biomedical Sciences and Human Oncology, University of Bari 'Aldo Moro', Bari, Italy

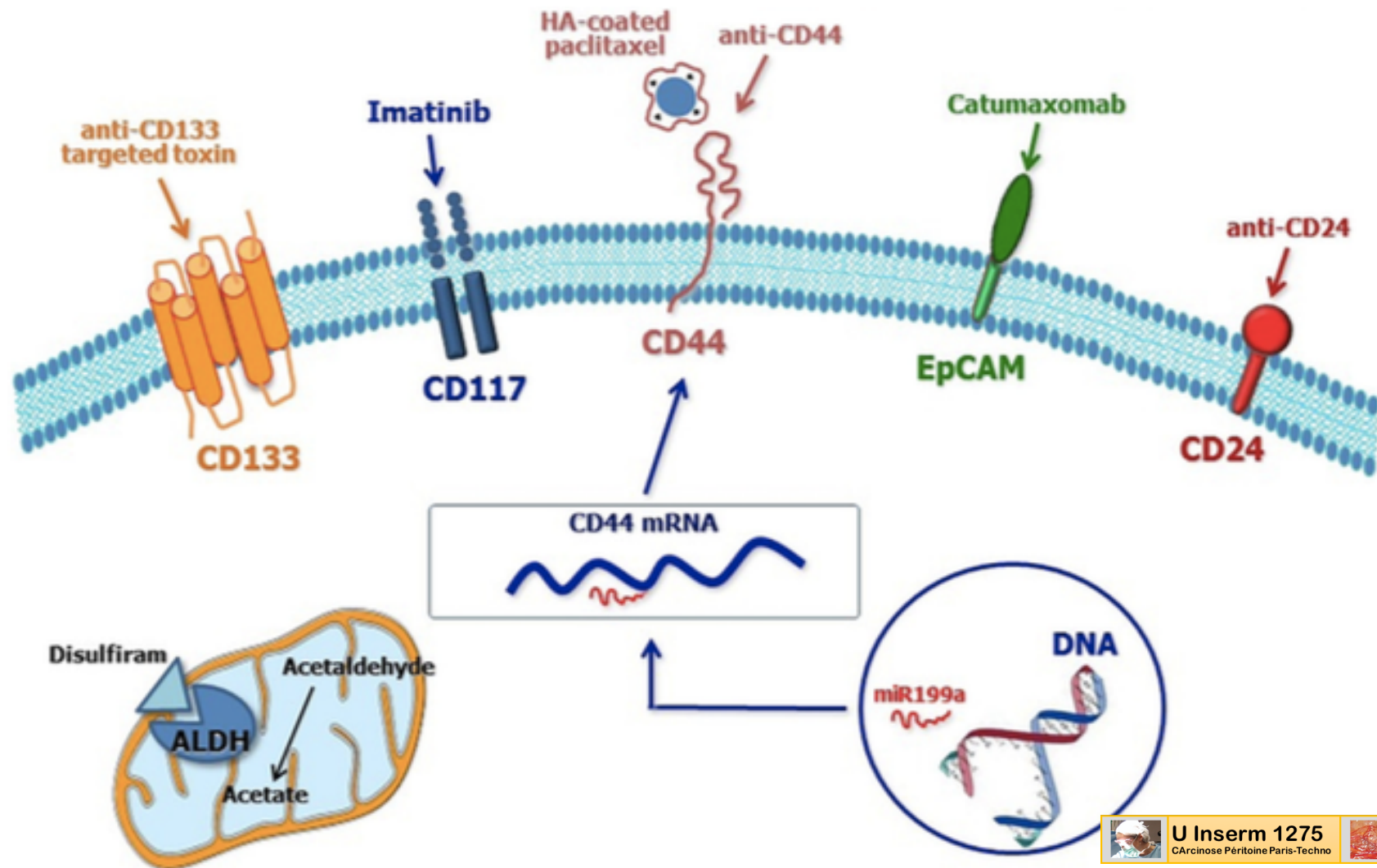
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R. Palmirotta et al. / Critical Reviews in Oncology/Hematology 117 (2017) 12–29



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www.impactjournals.com/oncotarget/

Oncotarget, 2016, Vol. 7, (No. 50), pp: 82741-82756

Research Paper

Is ovarian cancer a targetable disease? A systematic review and meta-analysis and genomic data investigation

Nicoletta Staropoli^{1,*}, Domenico Ciliberto^{1,*}, Silvia Chiellino¹, Francesca Caglioti¹, Teresa Del Giudice¹, Simona Gualtieri¹, Angela Salvino¹, Alessandra Strangio¹, Cirino Botta¹, Sandro Pignata², Pierfrancesco Tassone^{1,*}, Pierosandro Tagliaferri^{1,*}

Individualized treatment for ovarian disease control using PIPAC as neo adjuvant treatment

Background:

Recently treatment of ovarian cancer as gained in solidity regarding surgery protocol.

Surgical resection had to be complete (reported as a CC0 resection)

Cytoreductive surgery CRS

And done directly as the first part of the treatment or after a neo-adjuvant chemotherapy with **Carbo-Platin chemotherapy**

and had to be followed by intraperitoneal chemotherapy including **HIPEC**.

N ENGL J MED 378;3 NEJM.ORG JANUARY 18, 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer

W.J. van Driel, S.N. Koole, K. Sikorska, J.H. Schagen van Leeuwen,
H.W.R. Schreuder, R.H.M. Hermans, I.H.J.T. de Hingh, J. van der Velden,
H.J. Arts, L.F.A.G. Massuger, A.G.J. Aalbers, V.J. Verwaal, J.M. Kieffer,
K.K. Van de Vijver, H. van Tinteren, N.K. Aaronson, and G.S. Sonke



U Inserm 1275
Carcinose Péritoine Paris-Techno



Individualized treatment for ovarian disease control using PIPAC as neo adjuvant treatment

Background:

First part of the treatment is very define – no possibility to change the milestone of the treatment

Laparoscopy is done first to evaluate the extension of the disease

Cure had to be obtained at first line, after the death is the rule

Individualized treatment had to be proposed at the First line

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Cancer Sci 107 (2016) 1173–1178

Cancer Science

Japanese Cancer Association



Open Access

Review Article

Ascites modulates cancer cell behavior, contributing to tumor heterogeneity in ovarian cancer

Soochi Kim,^{1,2} Boyun Kim^{2,3} and Yong Sang Song^{1,2,4,5}

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Expression profile of cytokine is specific in every serosa for cancers cells, as pleural or peritoneal. Intraperitoneal cytokine levels and detection were higher than serum levels. We well known that microenvironment is a fundamental aspect of ovarian cancer tumor progression. One of that major aspect is related with the effect of ovarian cancer affected patients ascites on cancer cells or mesenchymal cells activation in vitro. Effects are induced by a specific cocktail of different cytokines, that could be analyzed using cytokine array. **We postulated that it is possible to identify a limited number of specific cytokine combination and propose specific drugs association.**

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How to create the **Cytokine-Card for persolized medecine** in ovarian carcinomatosis

Page 155 IPSCM Busan meeting / Massoud Mirshahi

Major detected cytokines in ovarian plasma:
NGF family, VEGF family, adinopectin, pro-angiogenic factors,
MMP, TIMP and Immuno-Inflammatory cytokines

Cytokine in ascitis : to be more analyzed ...

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Select treatment using tumor biopsy analysis

Or Use NGS platform to identified biological pathway

JNCIJ Natl Cancer Inst (2017) 109(11): djx066

Tumor Microvessel Density as a Potential Predictive Marker for Bevacizumab Benefit: GOG-0218 Biomarker Analyses

Carlos Bais, Barbara Mueller, Mark F. Brady, Robert S. Mannel, Robert A. Burger, Wei Wei, Koen M. Marien, Mark M. Kockx, Amreen Husain, Michael J. Birrer; on behalf of the NRG Oncology/Gynecologic Oncology Group

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We could isolate after the first ovarian cancer evaluation using blood test, using ascites analysis and using tumor biopsy

It could be highly complex to deliver a mix of different drugs regarding pharmacokinetic interaction and a major risk of toxicity.

That toxicity is the major risk regarding carcinomatosis affected patient, having physical status alteration and altered nutritional status.

One of the solutions could be **association of loco regional treatment with limited systemic drugs passage and intravenous classical drug administration.**

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Purpose:

Individualized neo adjuvant treatment to

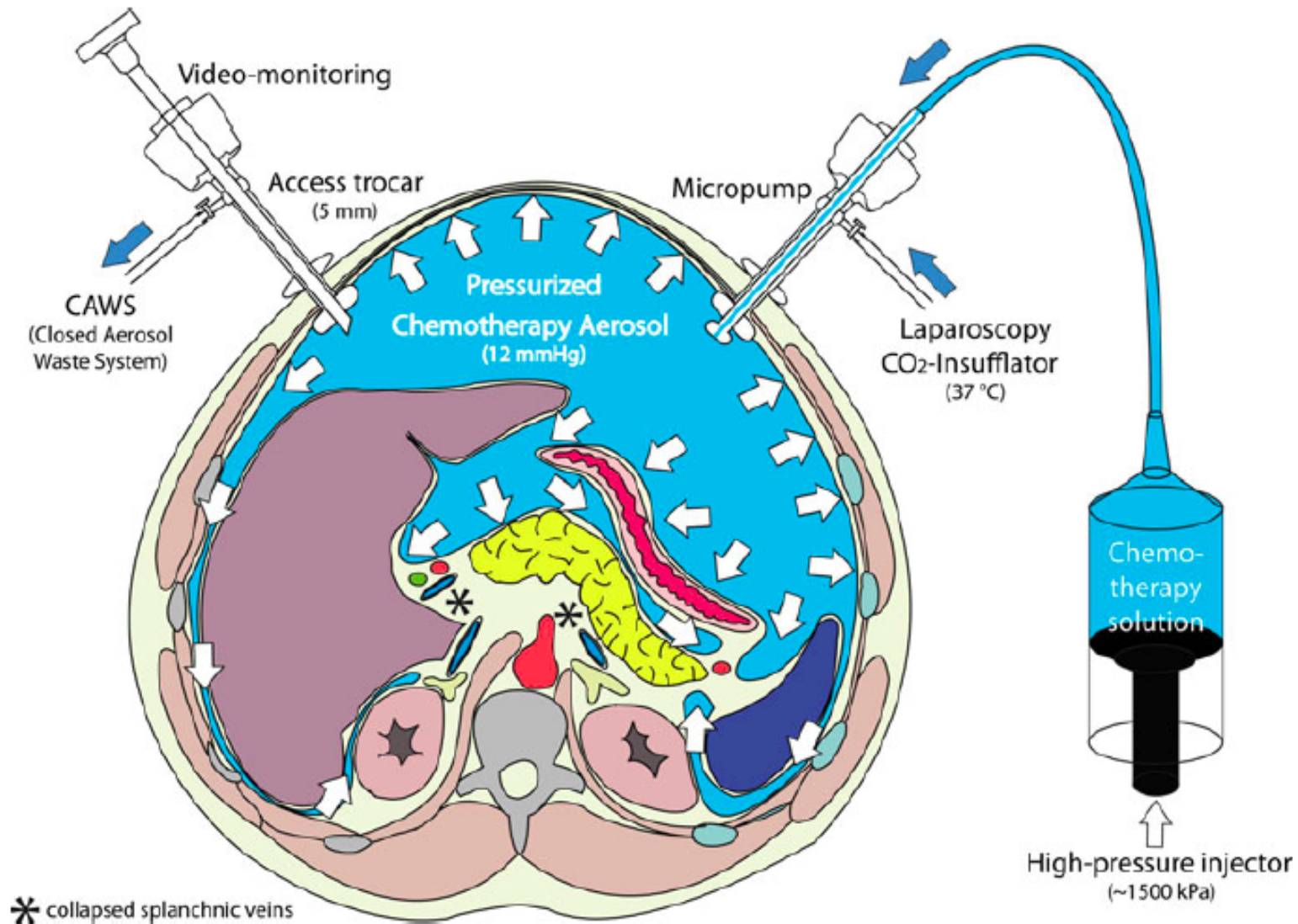
- increase tumor response
- Decrease aggression of surgery but with a complete cytoreductive surgery
- Associate another way to deliver chemotherapy and targeted therapy

Individualized treatment for ovarian disease control using PIPAC as neo adjuvant treatment

A technical solution could be proposed to obtain that result using **pressurized intraperitoneal aerosol chemotherapy** (PIPAC) technique. The combination of PIPAC and intravenous drugs is possible.

The PIPAC process offers another interesting aspect with the possibility to perform histological sequential analysis to confirm or not a tumor effect. That point is highly important because the evaluation of any treatment in case of peritoneal metastasis is very difficult using CT scan or other imaging procedure.

Pressurized intrapéritoneal Aerosol chemotherapy as PIPAC



1st PIPAC Nov 5th, 2011

Bielefeld Deutschland



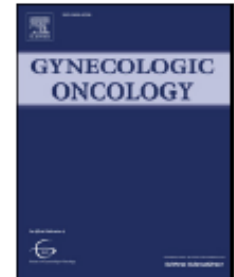
PIPAC



Contents lists available at [ScienceDirect](#)

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno



Activity of Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) with cisplatin and doxorubicin in women with recurrent, platinum-resistant ovarian cancer: Preliminary clinical experience

Clemens B. Tempfer^{a,*}, Ilknur Celik^a, Wiebke Solass^b, Bernd Buerkle^a, Urs G. Pabst^b, Juergen Zieren^b, Dirk Strumberg^c, Marc-André Reymond^b

^a Department of Obstetrics and Gynecology, Ruhr University Bochum, Bochum, Germany

^b Department of Surgery, Ruhr University Bochum, Bochum, Germany

^c Department of Hemato-Oncology, Ruhr University Bochum, Bochum, Germany

Gynecol Oncol.
2014;132(2):307-11



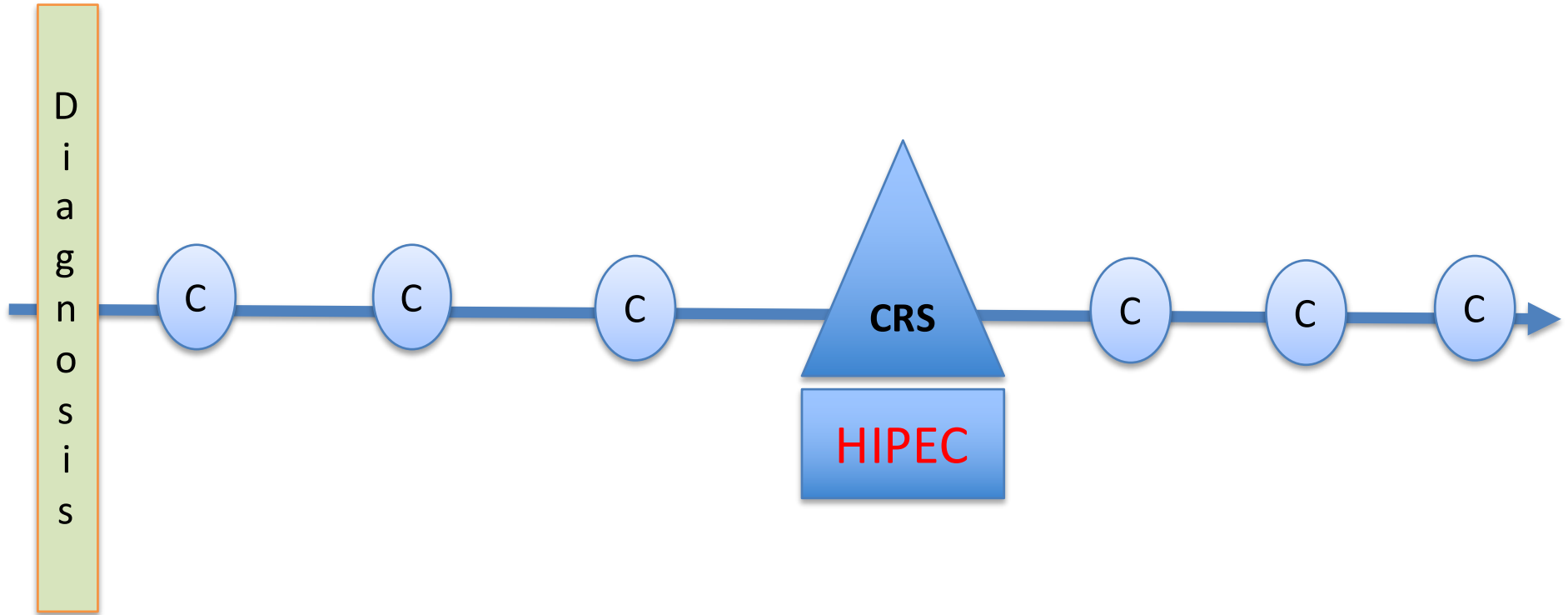
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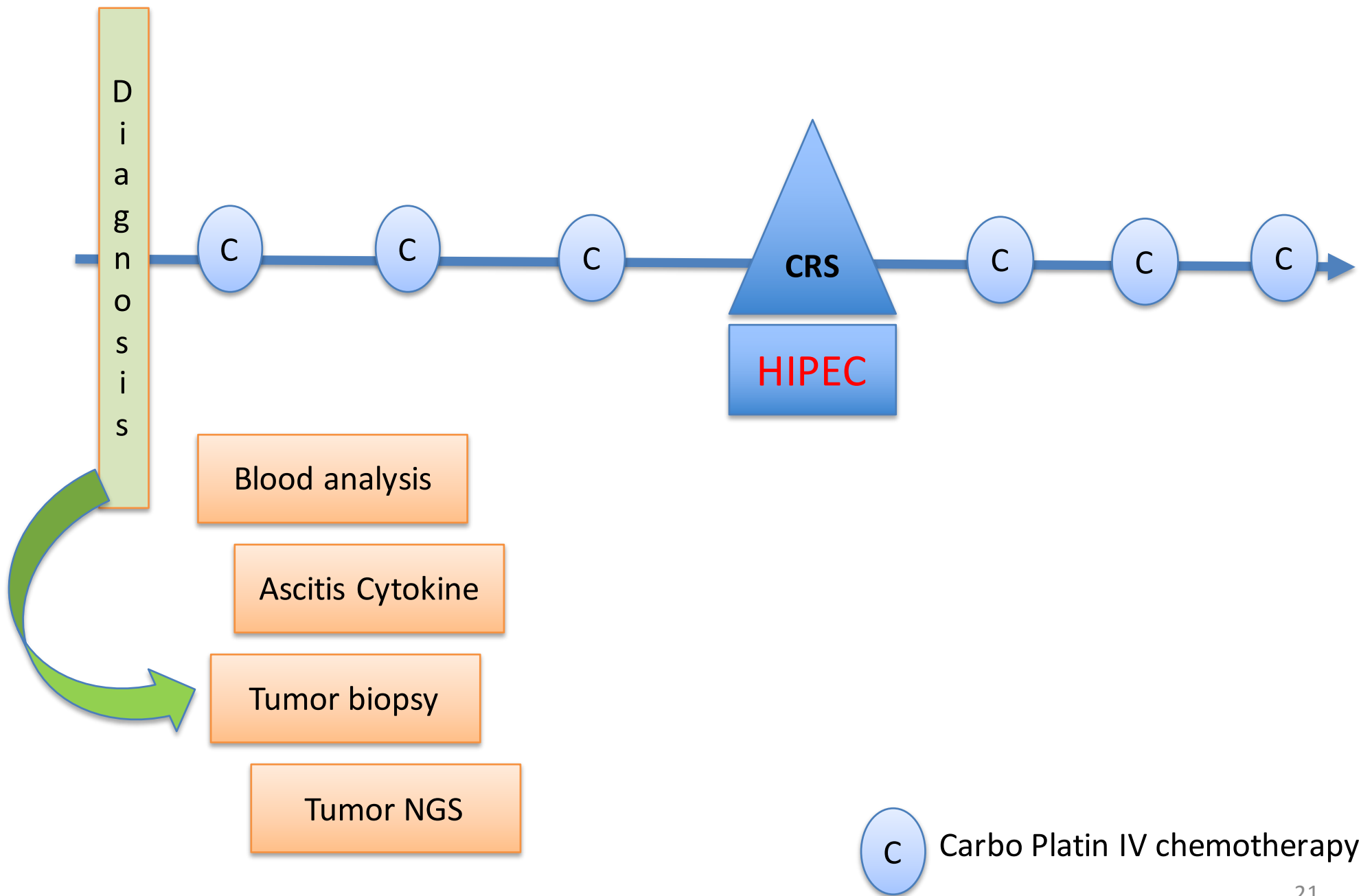
Pressurized intraperitoneal Aerosol chemotherapy

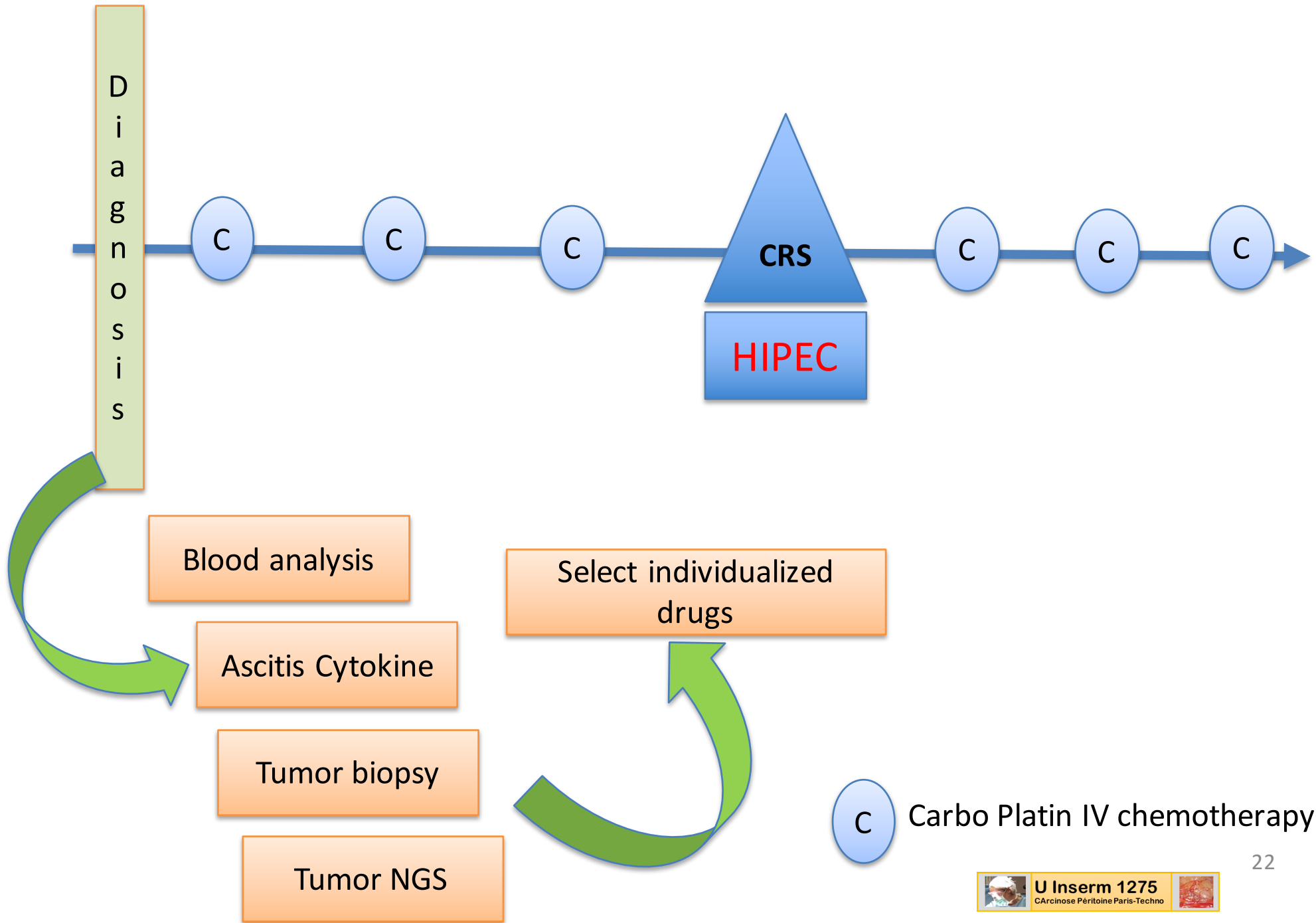


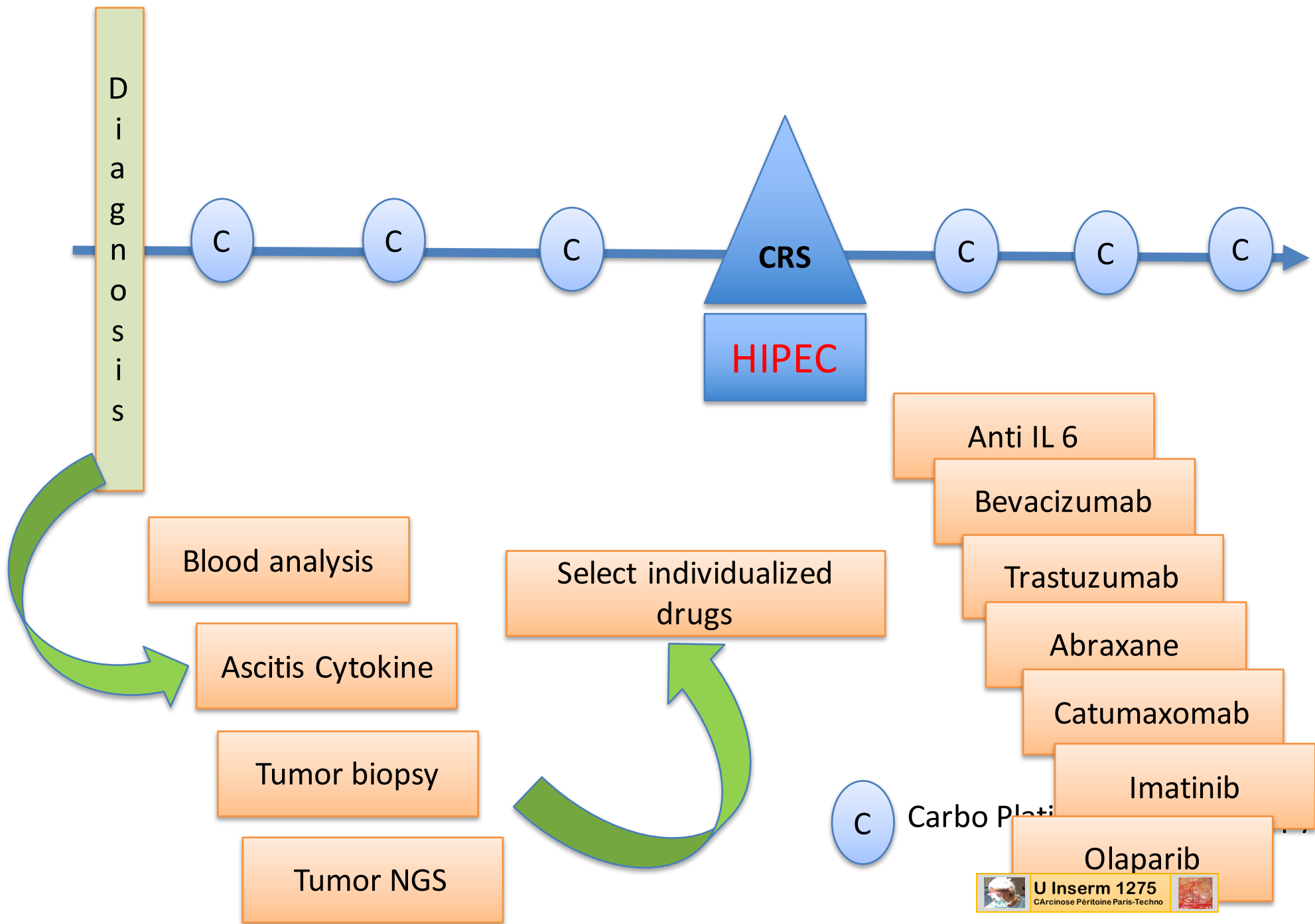
- Technology is more simple
- Aerosol delivery system is derived from car industry, from a common rail injector
- Any drug can be transformed in aerosol
- Drug volumes up to 200 ml
- More than 3000 procedures performed in the World



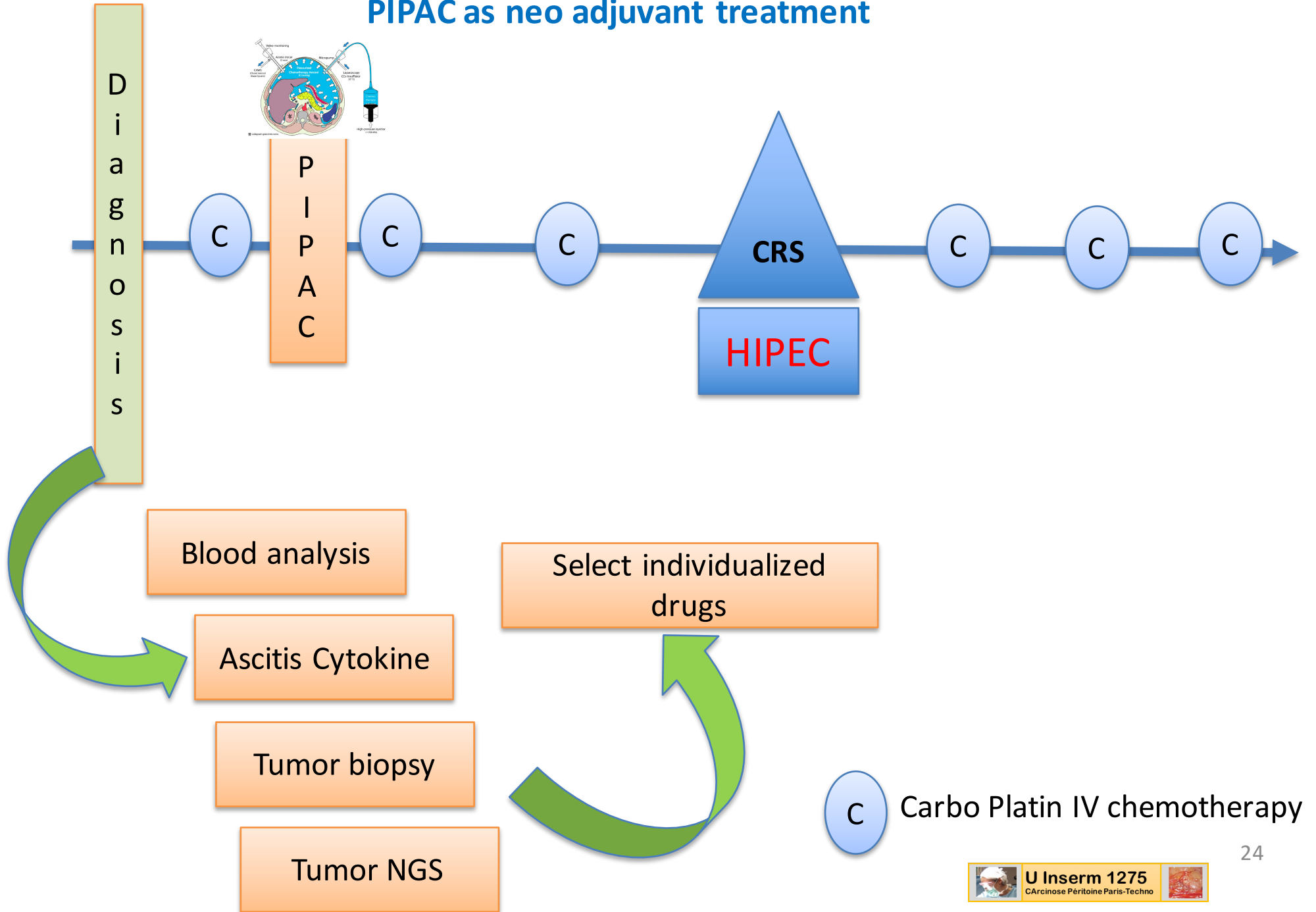
 Carbo Platin IV chemotherapy

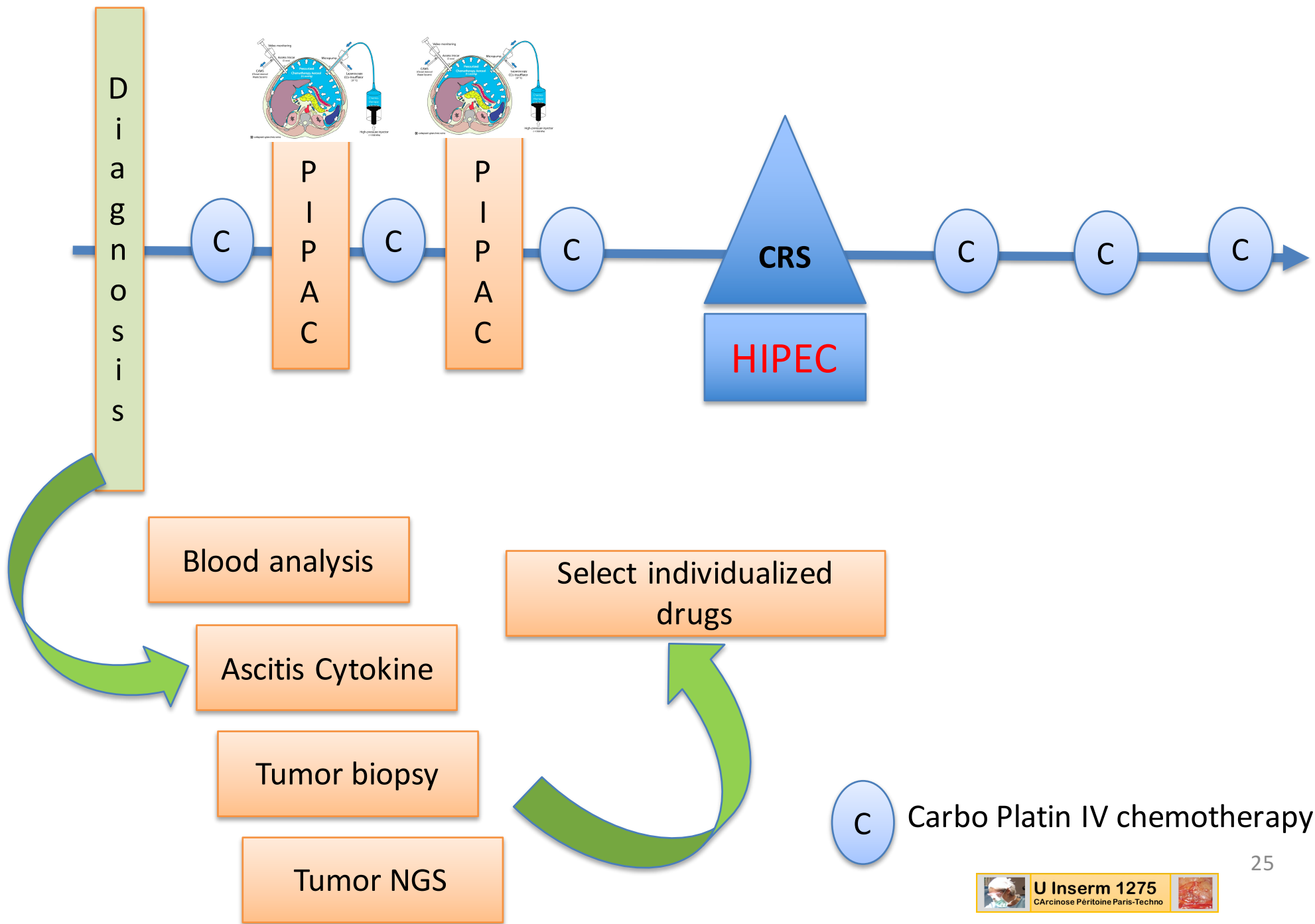




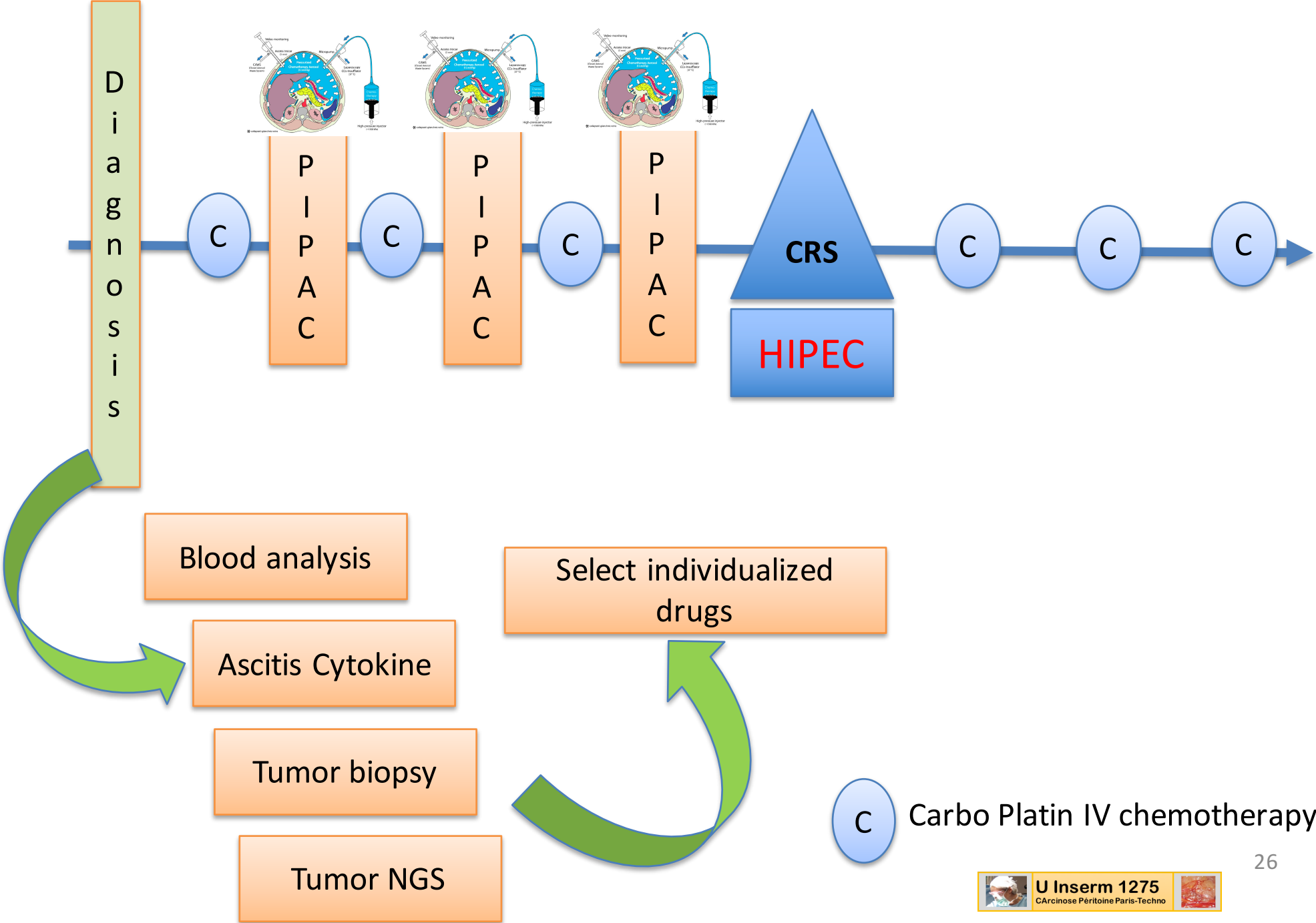


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We proposed to conduct a study to evaluate if a specific treatment could be proposed for patient affected by a peritoneal ovarian dissemination, first or relapse. The treatment final strategy could be:

1/ first a laparoscopic procedure (to evaluate the carcinomatosis and obtain tumor biopsy + ascites liquid for cytokines, interleukins, and growth factors study).

2 : Start Carboplatin and taxol treatment –

3 : PIPAC using specific targeted therapy adapted to the patient- 3 cycles as CarboTaxol and PIPAC repeated –

4 : Surgical resection with CRS for CC0 with post resection HIPEC

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See you in Paris in September 2018



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on Peritoneal Surface Malignancy**

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