Response to neoadjuvant therapy (Non-core)

Histological assessment of chemotherapy response is only applicable to high grade serous carcinomas (HGSC) at this time. An initial study has tested and validated the prognostic significance of chemotherapy response criteria, and assessed reproducibility in two independent series of tubo-ovarian HGSC.[1,2] This three-tier scoring system (the Chemotherapy Response Score (CRS)) is reproducible, simple to apply in practice, and has been validated in an international multicentre study.[3] This is the grading system currently recommended by the International Collaboration on Cancer Reporting Ovary Carcinoma Dataset Authoring Committee (DAC). The method is as follows:

1. Scoring should be carried out on a single haematoxylin and eosin (H&E)-stained section (refer to discussion of omental sampling in **MACROSCOPIC DESCRIPTION OF OMENTUM**).
2. A single block of involved omental tissue that shows the *least* response to chemotherapy should be selected (if there is no residual omental tumour a CRS score of 3 is given - see Table 5).
3. The amount of *viable* tumour should be assessed; this may or may not show degenerative changes in the form of nuclear atypia, smudging of the nuclear chromatin and cytoplasmic clearing.
4. The presence of fibrosis may be helpful in marking the site of previous tumour infiltration:
    a. When found in the absence of tumour, fibrosis is likely to indicate regression.
    b. If fibrosis occurs in association with tumour, this may simply reflect tumour-associated desmoplasia rather than regression.
    c. However, when fibrosis in association with tumour is accompanied by an inflammatory response (so-called 'fibro-inflammatory' response – fibrosis with associated macrophages and a mixed population of inflammatory cells), this indicates regression.
    d. Psammoma bodies may mark the site of previous tumour and can sometimes appear more numerous because their density increases in areas where tumour has disappeared.
5. As a guide, >95% of tumour should be viable for a score of 1, and <5% for a score of 3.
6. In studies to date using this system or a closely related system, a difference in prognosis was shown only when tumours with a CRS score of 1 or 2 were compared with those having a CRS score of 3.[1,2] However, the DAC recommends use of the three-tier system to gather more data for future studies.
7. Note that this system has only been applied to HGSCs to date.
8. If the omental tissue appears normal, with neither tumour cells nor fibrosis, it is important to ascertain that there was omental involvement prior to the start of chemotherapy, that has completely regressed, by review of the clinical and radiological findings, before assigning a CRS score of 3. If there was no omental involvement prior to starting chemotherapy, then a CRS score cannot be applied.

Table 5: Chemotherapy response score (CRS).[1]

Score	Criterion	Tumour regression
1	Mainly viable tumour with no or minimal regression-associated fibro-inflammatory changes[a] limited to a few foci	No definite or minimal tumour response identified
2	Multifocal or diffuse regression-associated fibro-inflammatory changes,[a] with viable tumour ranging from diffuse sheets, streaks or nodules, to extensive regression with multifocal but easily identifiable residual tumour.	Moderate response identified
3	Mainly regression, with few irregularly scattered individual tumour cells or cell groups (all measuring less than 2 mm), or no residual tumour identified.	Marked response with no or minimal residual cancer

[a] Regression associated fibro-inflammatory changes: fibrosis associated with macrophages, including foam cells, mixed inflammatory cells and psammoma bodies; to be distinguished from tumour-related inflammation or desmoplasia.

References

1 Boehm S, Said I, Faruqi A, Gilks CB and Singh N (2014). Development of a response scoring system to quantify the effect of neoadjuvant chemotherapy in ovarian cancer - ovarian cancer response scoring (OCRS) study. *Mod Pathol* 27:276A.

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3 Cohen PA, Powell A, Böhm S, Gilks CB, Stewart CJR, Meniawy TM, Bulsara M, Avril S, Brockbank EC, Bosse T, de Azevedo Focchi GR, Ganesan R, Glasspool RM, Howitt BE, Kim HS, Lee JY, Le ND, Lockley M, Manchanda R, Mandalia T, McCluggage WG, McNeish I, Midha D, Srinivasan R, Tan YY, van der Griend R, Yunokawa M, Zannoni GF and Singh N (2019). Pathological chemotherapy response score is prognostic in tubo-ovarian high-grade serous carcinoma: A systematic review and meta-analysis of individual patient data. *Gynecol Oncol* 154(2):441-448.