A panel discussion of controversies and challenges in the adjuvant treatment of colon cancer

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Current issues of adjuvant therapy for colon cancer concern the introduction of drugs other than fluorouracil-leucovorin (5-FU/LV), the benefits for stage II patients, the use of new primary endpoints and the influence of age on treatment benefits. These issues were addressed in a panel discussion and the conclusions were the following: FOLFOX4 is the first regimen that shows superiority over 5-FU/LV. The use of 3-year disease-free survival as primary endpoint could encourage the quicker adoption of improved therapeutic strategies into clinical practice. Available data suggest that there are some benefits for stage II patients, and the decision needs to be individualised for each patient. Further, therapeutic decisions based solely on the patient’s age are inappropriate, and geriatric assessment tools will help in making this decision. This information would improve patient and physician understanding of the recent data regarding the potential benefits of adjuvant therapy.

Keywords: adjuvant treatment, colon cancer.

Discusión de expertos sobre controversias y retos en el tratamiento adyuvante del cáncer de colon

Las controversias actuales referentes al tratamiento adyuvante del cáncer de colon incluyen la introducción de fármacos más allá de 5-FU/LV, el beneficio que ofrece a los pacientes con estadio II, el uso de nuevas variables y la influencia de la edad sobre los beneficios del tratamiento. Estas controversias fueron discutidas en un panel de expertos y las conclusiones fueron las siguientes: FOLFOX4 es el primer régimen que ha demostrado superioridad frente a 5-FU/LV. El uso de la supervivencia libre de enfermedad a 3 años como variable principal de los estudios podría permitir una adopción más rápida de estrategias terapéuticas. Los datos disponibles sugieren que existe beneficio para los pacientes con estadio II, y la decisión terapéutica debe ser individualizada. Finalmente, también se llegó a la conclusión de que las decisiones basadas únicamente en la edad no son apropiadas, y las herramientas de valoración geriátrica servirán de apoyo. Esta información puede mejorar el entendimiento de pacientes y médicos acerca de los datos recientes relativos a los beneficios del tratamiento adyuvante.

Palabras clave: tratamiento adyuvante, cáncer de colon.

IMPLICATIONS OF RESULTS OF THE MOSAIC PHASE III CLINICAL TRIAL

The primary curative therapy of colon cancer is surgical resection. However, within the last 15 years, prospectively randomized appropriately powered cli-
nical trials have convincingly demonstrated that pos-
teresection treatment, termed adjuvant therapy, is of
benefit to all patients with node-positive disease (sta-
ge II) and arguably to high-risk node-negative (stage
II) cases. The predominant single agent used as ad-
juvant therapy in colon cancer has almost universally
been fluorouracil (5-FU).
Attempts at modulating the activity of 5-FU with ot-
er compounds have been tried. A possible benefit
from the use of levamisole in combination with 5-FU
was suggested by a report from the North Central
Cancer Treatment Group (NCCTG) and confirmed
by the Intergroup study from the USA and a Dutch
trial. The evidence that adjuvant therapy is effective
in colon cancer was further demonstrated by contro-
nelled studies that compared 5-FU-leucovorin (LV)
(folic acid) treatment for 6 or 12 months. On the other
hand, although there is no internationally accepted
gold-standard 5-FU/LV regimen, the monthly 5-day
bolus North Central Cancer Treatment Group/Mayo
Clinic regimen has been commonly used as a refe-
rence treatment in phase III trials. However, when
this regimen was compared with LV5-FU2, a bimon-
thly schedule of LV and bolus-plus-infusion 5-FU for
2 consecutive days every 2 weeks in the metastatic
setting, LV5-FU2 proved superior in terms of respon-
se rate, progression-free survival, and toxicity, but
not overall survival. Moreover, when this regimen
was compared with the Mayo Clinic regimen in the
adjuvant setting, toxicities were significantly lower
in the LV5-FU2 group.
A number of new agents of interest in colorectal can-
cer have been recently tested in clinical trials inclu-
ding the platinum compound oxaliplatin. Although it
has been demonstrated that both cisplatin and carbo-
platin have no efficacy in advanced colon cancer,
oxaliplatin—a platinum analogue with clinically
significant renal and bone marrow toxicity—does ha-
ve activity in advanced colon cancer. Oxaliplatin has
been shown to enhance the response rate obtained
with 5-FU, although limiting toxicities were neutro-
penia and peripheral neuropathy.
In a phase III study, the effect of combining oxalia-
platin with LV5-FU2 was assessed in 420 previously un-
treated patients with advanced measurable disease
randomized to receive LV and bolus-plus-infusion 5-
FU, either alone or combined with oxaliplatin (85
mg/m² as a 2-hour infusion on day 1). Patients allo-
cated to oxaliplatin plus LV5-FU2 had significantly
longer progression-free survival and better response
rate when compared with the control arm. The im-
provement in overall survival did not reach signifi-
cance probably due to the second-line treatments ef-
fected by LV5-FU2 plus oxaliplatin produced higher rates
of neutropenia, grade 3/4 diarrhea, and grade 3 neu-
ro sensory toxicity, but this did not result in impair-
ment of quality of life. In a recent randomized contro-
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