Colorado Senate Bill 09-250

CONCERNING HEALTH BENEFIT PLAN COVERAGE FOR ORAL ANTICANCER MEDICATION.

Expert Opinion

Version March 27, 2009

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As the bill correctly states, viewing orally administered and IV anti-cancer medication on the same level is only justified if orally administered chemotherapy has been demonstrated to be equivalent. Based on a careful literature review, it can be stated that this is not the case and that oral cancer therapeutics still have risks that are not yet fully understood. It is interesting to note that, to the best of my knowledge, there are no studies in the literature that even directly compare therapeutic efficacy of oral and IV anti-cancer medication directly.

As of today, use of oral chemotherapeutics has the following unresolved problems:

- pills put the patient in the driver's seat and compliance becomes an issue. A recent meta-analysis has shown that compliance can be as low as 16%. It is known that patient who refill less than 70% of their oral cancer prescription have a significant higher incidence of death. Another very serious problem is overcompliance. Patients have been found to intentionally overdose to ensure efficacy even in the presence of severe toxicities. Injectables give the physician control over drug administration.

- Therefore, oral chemotherapy requires just as much care as intravenous chemotherapy and probably requires more attention to patient education and involvement in care decisions.

- After oral administration, the anticancer drug is subject to substantial inter-individual variability of its oral bioavailability. The reason is that the drug has to pass through the gut wall and the liver (these are full of drug metabolizing enzymes and drug transporters—this is called the "first pass effect"). Variable oral bioavailability is associated variable exposure. Low exposure increases the risk of treatment failure, high exposure the risk of toxicity. An injectable has always 100% bioavailability and the physician is in much better control of drug exposure than after a pill.

- Oral chemotherapeutics tend to cause more GI toxicity. The reason is quite simple-chemotherapeutics inhibit cell growth. The gut mucosa relies in fast growing cells. If an oral chemotherapeutic causes diarrhea this will significantly reduce its absorption and thus its efficacy. Drug exposure after administration of injectable is completely independent of GI toxicity or diarrhea.

- The effect of oral chemotherapeutic agents for the treatment of colorectal cancer has long been questioned in Western countries. These agents have been used for a long time only in Japan, and even among Japanese clinicians, skepticism was expressed about the benefits of these oral anticancer agents. At the beginning of the 21st century, however, these views were drastically changed by the evidence demonstrated by several clinical trials and meta-analyses. Although several oral chemotherapeutics are meanwhile approved in the US, there is still no convincing evidence that they are as good as injectables. What in light of the literature is very worrisome is that this bill addresses oral chemotherapeutics in general. Based on the literature, some oral anticancer drugs may have acceptable efficacy under controlled study conditions, but others clearly are inferior compared to injectables, must still be considered an experimental treatment and further clinical evidence will be required.