OncoVAX®

HEALTH TECHNOLOGY ASSESSMENT SECTION
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DISCLAIMER

Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. It is not subjected to an external review process. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

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DISCLOSURE

The author of this report has no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia

EXECUTIVE SUMMARY

Introduction
Colon cancer is one of the most common malignancies in the world. In recent years, there is a decline in death rates of colon cancer in the United States due to earlier detection of primary tumours. The most important prognostic indicator for patients with colon cancer is stage of disease at diagnosis. Accurate staging is essential to the appropriate therapeutic recommendation. Surgery is the primary modality for this disease. However, by the time patient presents with recurrent symptoms, the curable rate by surgery is poor even when combined with other therapy. There is an urgent need to develop effective treatment strategies to reduce morbidity and mortality from colon cancer.

Objective/Aim
To determine the safety, effectiveness and cost effectiveness of of OncoVAX® as vaccine for Stage II colon cancer.

Results and conclusion
There is limited poor quality evidence on the safety, effectiveness and cost-effectiveness of OncoVAX. Furthermore, OncoVAX is still undergoing phase IIIb clinical trial.

Recommendation
Based on the above review, the use of OncoVAX® for the treatment of Stage II colon cancer is not recommended until more high quality clinical evidence is available. Its use can only be recommended in research environment.

Methods
Scientific electronic databases searched include Pubmed, Proquest, EBSCO Host, Medline, CINAHL, Science Direct, Cochrane database of systematic reviews, HTA databases, Horizon scanning databases and FDA website were searched.

OncoVAX®

1. INTRODUCTION

Colon cancer is one of the most common malignancies in the world. The risk of colon cancer increases after the age of 40 and rises exponentially from the ages of 50 to 55; the risk doubles with each succeeding decade. In recent years, there is a decline in death rates of colon cancer in the United States due to earlier detection of primary tumours via stool blood tests, sigmoidoscopy, colonoscopy, and screening tests for serum carcinoembryonic antigen concentration levels.[1]

The most important prognostic indicator for patients with colon cancer is stage of disease at diagnosis. Accurate staging is essential to the appropriate therapeutic recommendation. Stage is determined by the depth of tumor penetration or invasion of the bowel wall, the number of lymph nodes involved, and the presence or absence of distant metastases.[2] Surgery is the primary modality for this disease. However, by the time patient presents with recurrent symptoms, the curable rate by surgery is poor even when combined with other therapy. When tumours are detected at localized early stage, the 5-year survival rate for colon cancer is greater than 90%. However, the rate drops to 40-65% when the cancer has spread regionally and involves adjacent organs or lymph nodes. For persons with distant metastases, 5-year survival is only 11%. Therefore there is an urgent need to develop effective treatment strategies to reduce morbidity and mortality from colon cancer.[1]

This technology review was conducted following a request from Director of Medical Development Division.

2. OBJECTIVE/AIM

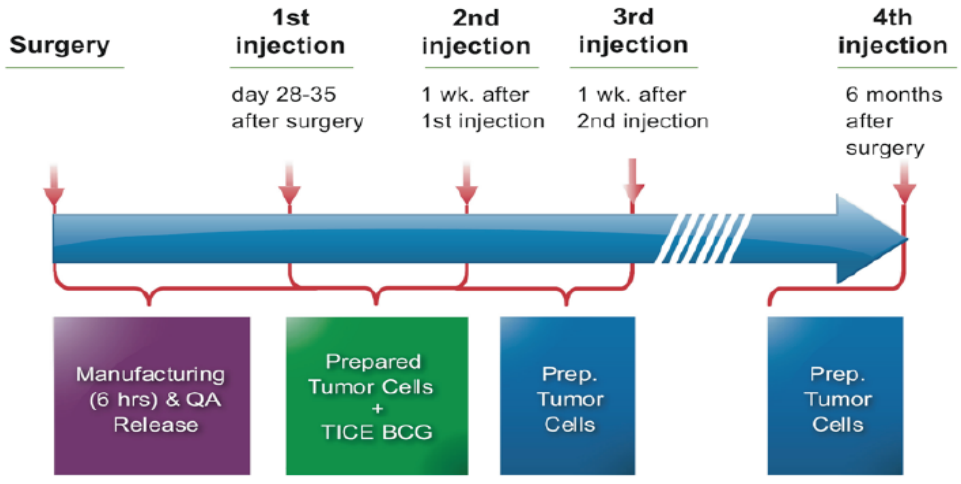
The objective of this review was to determine the safety, effectiveness and cost effectiveness of OncoVAX® as vaccine for Stage II colon cancer.

3. TECHNICAL FEATURES

OncoVAX® is an active specific immunotherapy (ASI) for the treatment of Stage II colon cancer. It is patient specific therapy as it uses the patient's own (autologous) tumour to prevent the recurrence of colon cancer following surgery. The vaccine is claimed to comprise of sterile, metabolically active, irradiated, non-tumorigenic autologous tumour cells, with or without fresh frozen bacillus Calmette-Guerin (BCG) bacteria as an adjuvant. Following surgery, the tumour is processed at the manufacturing site.

Fig 1: Schematic for OncoVAX® preparation

The vaccine is then injected intradermally into patient in four doses over the first six months after the surgery. The injections produce a delayed-type hypersensitivity response which indicates that the body's own T-cells will respond to tumour antigens. OncoVAX® has not obtained CE Marking or FDA approval. Currently OncoVAX® has undergone Phase IIIa trial. It has received Special Protocol Assessment and Fast Track Designation from FDA for the upcoming Phase IIIb trial.



4. METHODOLOGY

4.1. Searching

Electronic databases which include Pubmed, Proquest, EBSCO Host, Medline, CINAHL, Science Direct, Cochrane Database of Systematic Reviews, HTA Databases, Horizon Scanning databases and FDA website were searched. There was no limitation in the search. The following keywords were used either singly or in combinations: OncoVAX, active specific immunotherapy, vaccine, colon cancer, autologous tumour.

4.2. Selection

All published articles related to safety, effectiveness, and cost effectiveness of OncoVAX® or active specific immunotherapy in colon cancer were included. Studies related to vaccine use in other cancers were not included. Critical appraisal of relevant literature was performed and evidence graded according to Jadad Score (Appendix 1).

5. RESULTS AND DISCUSSION

The search strategy yielded three articles on OncoVAX®; three randomised control trial. However, assessment using Jadad Score indicate the studies to be of low quality evidence.

5.1. SAFETY

The vaccination schedule in the study by Vermorken *et al*. involved one intradermal vaccination per week for 2 weeks with about 10^7 viable, irradiated autologous tumour cells and 10^7 viable fresh-frozen BCG organisms. At 3 weeks and 6 months, patients received one vaccination of about 10^7 irradiated tumour cell alone. More than 93% of patients developed some degree of ulceration at the first two vaccination sites, most of which healed within 3 months. Eight patients did not receive BCG in their second vaccination due to severe reactions at the first vaccination site. Reactions to the third and fourth vaccines, without BCG, were of short duration, and ulceration occurred in only 7% and 4% of patients, respectively. Swelling of the lymph nodes closest to the vaccination site was more frequently seen with vaccines containing BCG and occurred in 66% of patients. Systemic reactions, including fever, chills, or both in the first 24 h occurred more frequently with the BCG vaccines than with the vaccines without BCG (mild reactions 22 vs 7%; severe reactions 5 vs 0.5%). No patient refused vaccination because of side-effects, and none needed to be admitted.[3]

In study by Harris *et al*. patients randomized to the treatment arm of the study received the vaccine intradermally in the right anterior thigh 28 to 35 days postoperatively. Vaccination was repeated 1 week later in the left thigh. The following week, 10^7 irradiated tumor cells without BCG were given intradermally in the right deltoid. The adverse event attributable to the vaccine was a local reaction characterized by ulceration, drainage, and crusting. These reactions occurred in 162 (79%) of 205 of the vaccinated

patients and was described as mild, moderate, or severe in an equal number of patients. There were 15 patients with vaccine site infections: four cases with mild infection and 11 cases with moderate infection. All patients with local infections responded to oral antibiotics. None of the infections became systemic.[4]

5.2. EFFECTIVENESS

In a prospective randomized control trial by Hoover *et al*., statistically significant differences in overall survival (P=0.02) and disease-free survival (P=0.039) were seen in colon cancer patients treated with OncoVAX in comparison to those in control group. There was statistically significant difference in rate of recurrence of the primary tumour or occurrence of a second primary tumour between treated and control colon cancer patients (P=0.03; hazard ratio 2.97). There was no significant treatment difference in the rectal cancer patients.[5]

A phase III trial was conducted by Harris *et al.* to determine whether surgical resection plus active specific immunotherapy was more beneficial than resection alone in stage II and stage III colon cancer patients. On the basis of intent-to-treat analysis, there was no statistically significant difference between the two treatment arms in disease-free or overall survival or time to recurrence. In the same study, an analysis was performed to determine whether clinical outcome correlated with the degree of the induration to the third vaccination. Disease-free and overall survival was compared for patients in three groups: those with indurations to the third vaccination of < 5 mm, between 5-10 mm, and >10 mm. The proportion of patients surviving 5 years with an induration response of less than 5 mm was 45.0%; between 5-10 mm was 74.7%; > 10 mm was 84.6%. The differences in the 5-year survival and disease-free survival proportions for these three subsets of subjects were statistically significant (*k* exact test P =0 .003 for overall survival and P=0 .006 for disease-free survival). This indicates correlation between magnitudes of immune response to improved prognosis.[4]

Study by Vermorken *et al*. showed adjuvant OncoVAX® significantly reduced the rate of disease recurrence by 44% in patients with Stage II and Stage III colon cancer. The major impact was in Stage II disease where there was 61% risk reduction for recurrences (P=0.011) accompanied by a 42% risk reduction for recurrence free survival (P=0.032). There was a trend toward improved overall survival.[3]

5.3. COST / COST- EFFECTIVENESS

OncoVAX® had beneficial cost-effectiveness ratio as indicated by cost-effectiveness and cost-utility analysis. The analysis showed the costs per life year gained amounted to [redacted], costs per recurrence-free life year gained were [redacted], and costs per QALY amounted to [redacted].[6]

6. CONCLUSION

There is limited poor quality evidence on the safety, effectiveness and cost-effectiveness of OncoVAX. Furthermore, OncoVAX is still undergoing phase IIIb clinical trial.

7. RECOMMENDATION

Based on the above review, the use of OncoVAX® for the treatment of Stage II colon cancer is still under development stage and therefore, not recommended until more high quality clinical evidence is available. However, its use in research environment can be considered.

8. REFERENCES

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