Autologous Formalin-fixed Tumor Vaccine (AFTVac)
Induction of human autologous cytotoxic T lymphocytes on formalin-fixed and paraffin-embedded tumour sections

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Human autologous tumour-specific cytotoxic T lymphocytes (CTL) were generated from peripheral blood on small formalin-fixed paraffin-embedded sections of a gastric cancer. The CTL killed live target cells at an effector/target ratio of 1 within 24 hours and showed the same target specificity as those induced on live cancer cells. The killing activity of the CTL lasted for more than four months in culture and was inhibited by antibodies against CD8 and MHC-class I. These results suggest that adoptive immunotherapy of tumours will be possible with CTL induced on a stable source of tumour antigen.
Tumor-Associated Antigenic peptides (TAAs) in the formalin-fixed tumor-antigenic protein

Formalin cross linkage

TAAs, not destroyed
Autologous Formalin-fixed Tumor Vaccine (AFTVac)

Formalin-fixed tumor tissue

Injection

AFTV

Resection

Suppression of recurrence, metastasis, & remaining-tumor growth
Liver cancer
Truly effective?

Phase IIb randomized clinical trial on hepatocellular carcinoma (HCC)
Protocol

Surgery

DTH-1
erythema ?

AFTV

DTH-2

erythema measurement

Follow up
AFTVac prepared from the paraffin-embedded fixed tumor tissue
(DTH-1, before vaccination, negative)
During the vaccination

KUMA-1, New-Vac-2, 1st - 020424, 2wks later

2nd - 020508, 2wks later
AFTVac prepared from the paraffin-embedded fixed tumor tissue
(DTH-2, after vaccination, positive)

KUMA-1, DTH-2 (11 mm). New-Vac-2, 020607
Phase IIb, recurrence-free survival

Recurrence-free (%)

AFTVac
(n=18)

Control
(n=21)

Months

0 6 12 18 24

0 100

AFTVac
Control
After statistical analysis,

Log rank test, $p=0.003$

Clear suppression of recurrence of hepatocellular carcinoma
Large size HCC at the operation = High rate of recurrence

AFTVac → Recurrence

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Control</th>
<th>AFTVac</th>
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<tbody>
<tr>
<td>All patients</td>
<td>13/21 (62%)</td>
<td>3/18 (17%)</td>
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<tr>
<td>Tumor size</td>
<td></td>
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<tr>
<td>≥50 mm</td>
<td>10/11 (91%)</td>
<td>3/9 (33%)</td>
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*P value (Log rank test) 0.003*
Phase IIb, overall survival

![Graph showing overall survival for AFTVac and Control groups.]

- AFTVac (n=18)
- Control (n=21)

Overall Survival (%)

Months
Overall Survival

Log rank test, $p=0.01$

Injection of AFTVac after resection,

Yes, you can survive!
Liver cancer patient with hepatitis C

Liver cancer taken at the third time of surgery

Cancer cells, scattered throughout some liver
CMI0757  HCV infection  HCC, repeated recurrence

![Graph showing treatment timeline and AFP levels over time.]

- Total no. of treatments, 29 times
- No additional therapy since AFTVac
- 24 mo. from Ope-3 (18 mo. from AFTV), no more recurrence
- 7 mo. from Ope-2

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Brain tumor
59/M  Glioblastoma multiforme

Before operation
59/M  Glioblastoma multiforme

After operation  Radiation  12 months  24 months
+ AFTVac

Complete response

Lung cancer
Lung cancer 73/F who experienced bladder carcinoma 13 years ago.

2004. 7  Turbid pleural effusion with adenocarcinoma cells  →  Resection of right upper lobe

2004. 9  AFTVac without any other therapy

Three months after the vaccination, tumor markers decreased continuously for 7 months.
Non-small cell lung carcinoma, 73/F
who experienced bladder carcinoma 13 years ago.

2004. 7 Disruption of the lung tissue with turbid pleural effusion including adenocarcinoma cells

Resection of right upper lobe
CMI0144  Non-small cell lung carcinoma, 73/F

AFTVac monotherapy

Date (Mo.)

ng/ml

Surgery (VATS)

CEA

Vaccine

CYFRA
Any adverse effects?

We have experienced tumors of:

Brain, stomach, colon, liver, mammary, ovary, ......etc.

Adverse effects ( < CTC grade 2):
fever (temporal), pruritus, desquamation, erythema

but

No autoimmune disease.

Essentially no problem!
Breast cancer
Bone metastasis of breast cancer

- in the analysis of the total cases from 8051 non can be cured by radiation therapy
  (16 randomized trials, 20 prospective studies, 5 retrospective studies and 22 other articles) (Falkmer U, Acta Oncol 2003, 42:620–633.)

- healing with zoledronic acid in the aromatase inhibitor is hard to expect

- radiation therapy and refractory standard chemotherapy (CEF)
  (Kimura M, Breast Cancer 2010, 17:190–198.)

→ breast cancer bone metastases can’t be healed by one of these treatments
Breast cancer patients

Breast cancer bone metastases, no recovery with any treatment

Treatment: autologous cancer vaccine

- Radiation (36 Gy) + standard chemotherapy (cyclophosphamide, epirubicin, 5FU) + zoledronic acid
- Harmless adhesive (with administration despite the triple-negative habituation)

Cancer vaccine healed!
Primary peritoneal serous carcinoma
Peritoneal cancer: very similar to ovarian cancer

Standard therapy (paclitaxel-carboplatin)

• The treatment is impossible when it isn’t working correctly

Healed primary peritoneal cancer (PPSC)

Up to this point
TC therapy, 17 course, no longer – out of control

So TC therapy - added with autologous cancer vaccine while continuing
Primary serous peritoneal cancer (PPSC)
However, to our regret, we could not eradicate large tumor burden.

Need combination therapy with other methods radiation, chemotherapy, etc.
AFTVac, suitable application

![Graph showing the relationship between Tumor Growth Rate and Tumor Size, with AFTVac efficient area highlighted.](image)