PERSONAL RESPONSE TO TREATMENT

A NEW BLOOD BIOMARKER TO MONITOR TUMOR ACTIVITY [1] PROVIDES PHYSICIANS WITH KEY NEW INFORMATION:

hPG80

DIAGNOSIS | SURGERY MONITORING | ✓ TREATMENT MONITORING | RELAPSE MONITORING

hPG80 FOR TREATMENT RESISTANCE MONITORING

SCIENTIFIC & CLINICAL BACKGROUND

After several weeks, months or years, resistance to the treatment appears in many patients, causing a relapse. Resistance to treatment means that the drug is no longer effective in controlling the disease[1]. The resistance can be primary if the patient is resistant from the outset, or secondary if the treatment was initially efficient but became inefficient with time.
Resistance can occur when the target of the drug is altered by a mutation in the DNA of the tumor cells. This will limit the effectiveness of the initial treatment. It can also be the consequence of tumor heterogeneity, with a subset of tumor cells not able to respond to the treatment.

CHALLENGES

Early detection of treatment resistance is important to protect the patient from side effects, and to modify ineffective treatment for potentially effective treatment. It is also important to avoid unnecessary cost of inefficient treatments

OPPORTUNITIES

✓ **hPG_{80} is detected in the blood of 83% of all cancer patients, whatever the stage of the cancer. Its level varies upon disease evolution, making of hPG_{80} a biomarker capable of detecting treatment resistance**

hPG80 KEY FACTS

In cancer, hPG_{80} is overexpressed in the tumor and detectable in the patient's blood[2]

- ✓ **Cancer stem cells express elevated levels of hPG_{80} (circulating progastrin)[3, 4]**
- ✓ **Secretion of hPG_{80} maintain tumor-initiating and self-renewal capabilities of cancer stem cells[4]**
- ✓ **hPG_{80} (circulating progastrin) is released from the tumor and becomes detectable in the blood[4, 5]**
- ✓ **Plasma hPG_{80} is elevated in a wide range of cancer patients[1]**

hPG_{80} (circulating progastrin) is produced by all cancer cells, but in quantities 100 to 1000 times higher by cancer stem cells[3], making hPG_{80} the only blood biomarker that not only detect the presence but also the activity of the tumor.

hPG80 AND RESISTANCE TO TREATMENT HIGHLIGHTS

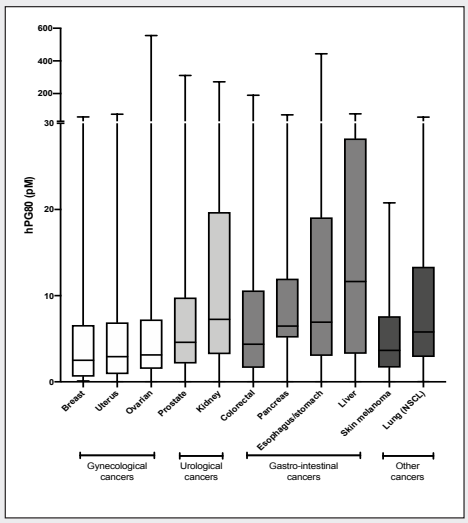
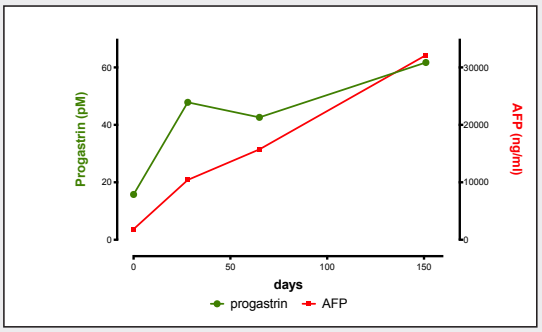


Figure 1.: Comparison of median hPG_{80} concentrations between all types of cancers tested: breast (n = 62), CRC (n = 305), esophagus/stomach (n = 74), kidney (n = 184), liver (n = 110), lung (n = 60), skin melanoma (n = 38), ovary (n = 44), pancreas (n = 34), prostate (n = 558), uterus (n = 77).

Figure 2.: hPG_{80} and AFP blood levels in an HCC patient treated with intra-arterial chemo-embolism, then radiofrequency and then NexavarR. The patient resisted to all the treatments as attested by the imaging follow-up, in agreement with the increased levels of hPG_{80} and AFP.

✓ hPG_{80} is expressed in multiple cancers (Figure 1)
If the patient is positive for hPG_{80} at diagnosis, variation of hPG_{80} level can be monitored all along patient's treatments.
When level increases during treatment, it is an indication of resistance as hPG_{80} is linked to the tumor activity.
In the example of Figure 2, the patient has a hepatocellular carcinoma (HCC). He is treated with intra-arterial chemo-embolism, radiofrequency and NexavarR. hPG_{80} level increased upon the first treatment and remained high thereafter. Disease progressed at all time points, indicating resistance to treatments. hPG_{80} kinetic was in agreement with that of alpha-foeto protein (AFP), showing the coherence of both biomarkers.



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PROGASTRIN cancer control association

Association of Health Professionals for Health Professionals

The Progastrin Cancer Control association has already published the white paper on the interactions between hPG_{80} (circulating progastrin) and cancer in French and English. This white paper can be downloaded from our website at:
https://www.progastrin-cancer-control.org

Any health professional can join the association.

Edited by Progastrin Cancer Control Association – 9, rue Boutard - 92200 Neuilly-sur-Seine - France – Registred at Préfecture des Hauts-de-Seine (FRANCE) — R.N.A. number W922012887

PERSONAL RESPONSE TO TREATMENT

A NEW BLOOD MARKER TO MONITOR TUMOR ACTIVITY [1]

hPG80

CLINICAL CASES ANALYSIS

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Case Report – Patient 1

This is a 69 years old patient diagnosed of locally advanced HCC with past medical history of a stent myocardial, a stroke and diabetes without signs of cirrhosis. The patient was treated with Nevaxar®. As he did not respond to the treatment, he then recei ved gemox, which stabilized the disease. hPG_{80} increased upon Nexavar® and returned to baseline upon gemox, when the patient responded to the treatment.

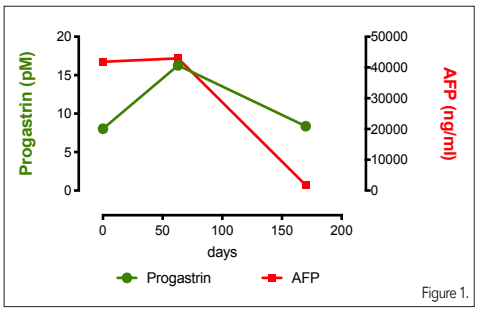


Figure 1.

This example shows that the kinetic of hPG_{80} variation follows disease evolution, as did AFP for this patient that was positive for AFP at baseline.

Case Report – Patient 2

This is a 56 years old man diagnosed with a multifocal HCC (3 nodules). The patient presented as medical history of type 2 diabetes and cirrhosis due to high alcohol consumption.
The patient was treated with 3 successive intra-arterial chemo-embolism rounds. The disease remained stable at the first treatment before regressing during the two others. At the control visit for surveillance, the CT scan showed a progression.

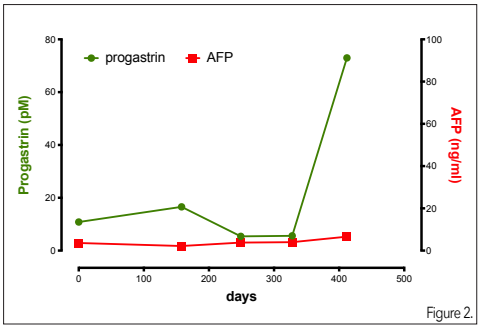


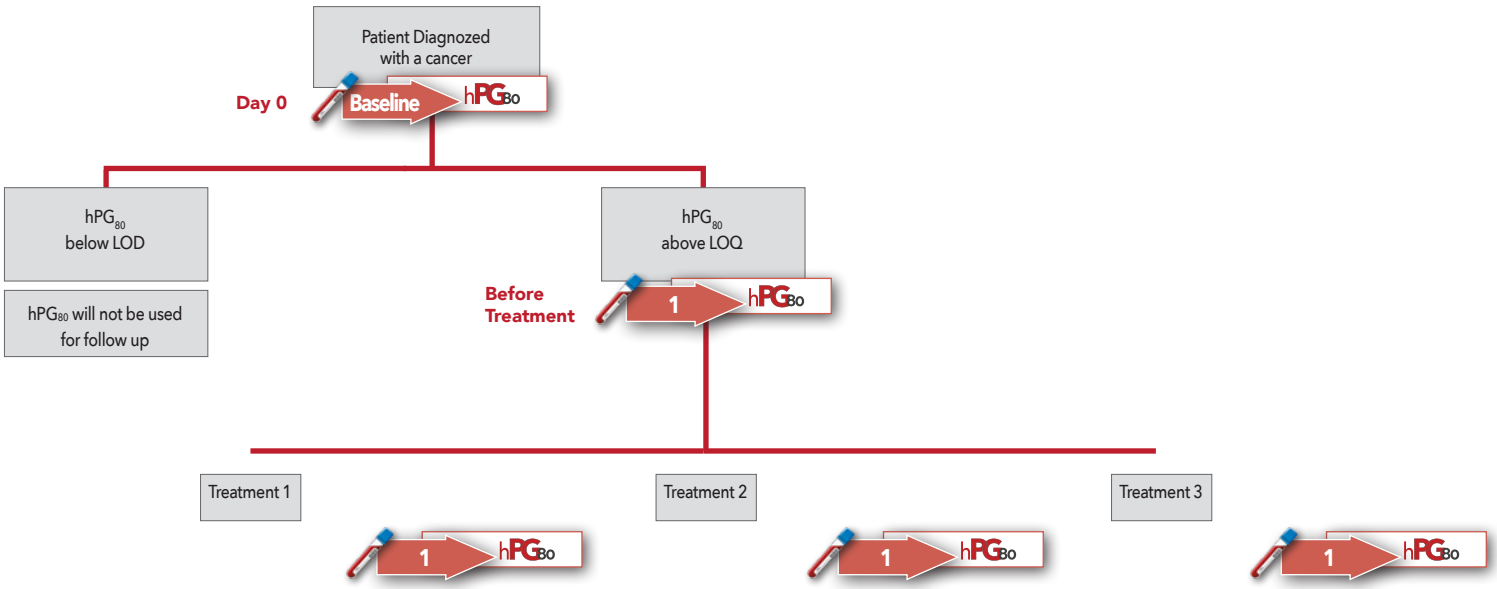
Figure 2.

Level of hPG_{80} followed disease evolution. After an initial slight increase from 10.8 to 16.6 pM when the disease was stable, it decreased up to 5.4 pM, but was still detectable. Upon clinical relapse, it increased up to 73 pM, showing an intense tumor activity.

AFP was below 20 ng/ml at all time points.
Therefore, for this patient, hPG_{80} provides a reliable information on disease evolution that AFP does not, suggesting strongly that hPG_{80} can be used for HCC patient follow-up, at least for those AFP-negative patients.

Dr. Thierry Cousin MD

SUGGESTED USE OF hPG80 FOR RESISTANCE TREATMENT MONITORING



- If the level of hPG80 remains high or increase, it suggests resistance to treatment.
- If there is another clinical observation leading to the same conclusion, change the treatment if possible.

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