trophoblastic tumour. These advances have become possible because of the ability to measure tumour load with hCG, diagnose hydatidiform mole in early pregnancy by ultrasound, and the ability to determine whether or not metastases are present on CT and MRI, together with greater understanding of the pathology and molecular physiology of trophoblastic neoplasia.6

Schmid and colleagues focus on a rare entity of trophoblastic neoplasia, which is placental-site trophoblastic tumour. The condition was first described in 1976 and named trophoblastic pseudotumour,7 and was thought to be benign. It was not until 1981 that Twiggs and colleagues5 encountered a patient who had metastases, and in 1982 Eckstein and colleagues8 reported four further cases from Charing Cross Hospital. Most reports since then have been case reports or the small number of patients that are cited in today’s report.

It is now accepted that placental-site trophoblastic tumours differ from other trophoblastic neoplasms in that the tumour load is not accurately correlated with the concentration of hCG, and that the tumour might be less sensitive to chemotherapy that is effective in the other types of trophoblastic neoplasia. Placental-site trophoblastic tumours might follow any type of pregnancy event, not infrequently becoming clinically apparent even years later, and there is great variability in its malignant aggressiveness. The neoplasm arises from intermediate trophoblast, unlike choriocarcinoma, which arises from villous trophoblast. There can be difficulty with the diagnosis if access to biopsy is not easy, and there is difficulty in histological differentiation of placental-site trophoblastic tumours from the other trophoblastic neoplasms. Unlike with postmolar trophoblastic neoplasia, precise histological diagnosis is essential. Immunohistological staining for human placental lactogen and hCG is especially helpful. Raised free β-hCG concentration in serum can also point to the diagnosis when germ-cell tumours of the ovary and other cancer entities can be excluded by clinical examination and imaging.10

What Schmid and colleagues show more convincingly than was previously evident is that the greater the interval between the index pregnancy and appearance of overt neoplasia, the more likely the disease will be aggressive. It is gratifying to find that the investigators advocate adjuvant chemotherapy even for stage I disease.

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NCT trial: more than a small victory over sleeping sickness

The natural history of central nervous system infection by Trypanosoma brucei gambiense consists of a distinctive neurological syndrome (sleeping sickness) proceeding to inevitable death. For more than 50 years intravenous melarsoprol has been the most common therapeutic approach, but this arsenical compound can cause a reactive encephalopathy with high risk of mortality and shows falling efficacy in certain areas.1 Efornithine is an efficacious alternative with fewer side-effects,2,3 but the need for its 6-hourly administration via slow infusion, over 14 days, has limited uptake in resource-poor settings. Oral nifurtimox shows too low an efficacy for routine use as monotherapy5 but has been tested recently in combination with efornithine,
yielding encouraging data on efficacy and side-effect profile.\textsuperscript{6–8}

In The Lancet today, Gerardo Priotto and colleagues\textsuperscript{9} present an open-label randomised trial comparing standard efomithine (400 mg/kg per day in 6-hourly infusions for 14 days) with nifurtimox-efomithine combination therapy (NECT: oral nifurtimox 15 mg/kg per day for 10 days, efomithine 400 mg/kg per day in 12-hourly infusions for 7 days) in adults with stage II African trypanosomiasis. Both the trial methodology and results are noteworthy. The study design was non-inferiority, a pragmatic decision in view of the predicted cure rate of more than 90%.\textsuperscript{10} Non-inferiority trials demand robust diagnosis, treatment, and follow-up (notoriously difficult in this context), because weak methodology tends to dilute differences in efficacy which increases the chance of a type I error (false conclusion of non-inferiority).\textsuperscript{11} In this regard, the study performed optimally with a completed follow-up rate of 93%, a truly remarkable figure in view of the logistical challenge of doing lumbar punctures over an 18-month period in nearly 300 patients living in remote communities.

As it turned out, in the planned primary outcome analyses of efficacy, NECT seemed superior to efomithine alone (cure rates of around 97% vs 92%). Even the worst-case sensitivity analysis, in which losses to follow-up were regarded as failures, confirmed non-inferiority. Adverse events were generally fewer in the NECT group. These findings suggest that NECT has typical advantages of a combination therapy: equivalent or improved efficacy and reduced side-effects. Furthermore, the reduced frequency, duration of course, and total quantity of efomithine infusion in NECT favour its use in resource-poor settings, in view of the savings in transport and equipment costs as well as staff time. On theoretical grounds, the combination should inhibit the development of resistance to the individual component drugs, as seen for various other infections.

WHO has already endorsed the study’s findings by entering NECT into its Essential Medicines List. It should be pointed out that there has not been a direct comparison of NECT with melarsoprol, or nifurtimox-melarsoprol, a combination favoured by some practitioners that proved efficacious in another large trial.\textsuperscript{5} However, we believe that there is now a strong evidence base to support promotion of NECT within national treatment strategies.

Despite the optimism generated by today’s trial, innumerable challenges remain, including the urgent need to develop improved treatments for the earlier haemolymphatic phase (stage I) of African trypanosomiasis. Despite best efforts, there are still no reports of successfully completed phase III randomised trials in stage I, in which treatment (pentamidine administered by 7–10 daily intramuscular injections) has also remained unchanged for half a century. In our experience it is paradoxically more difficult to recruit and follow up patients with milder clinical manifestations than those in stage II disease, and these studies will require particularly intense support from sponsors and collaboration from all partners. There is also room to refine diagnosis as well as develop coherent strategies for control and surveillance.

Today’s study with NECT shows the way forward, setting a high bar in terms of trial methodology that other studies should aim to replicate. The success of this study depended on collaboration between a wide variety of agencies, including the Drugs for Neglected Disease Initiative and Médecins Sans Frontières (the trial’s sponsors), several academic centres, and the national trypanosomiasis programmes of the Republic of the Congo and the Democratic Republic of the Congo. Fundamentally, this project builds on the efforts of countless individuals in sleeping sickness teams across Africa who work in indescribably difficult conditions year after year with a positive and indomitable spirit.\textsuperscript{12} This potent combination
has produced a study that in every respect rivals those in
diseases for which research receives vastly superior funds.

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G8 Summit 2009: what approach will Italy take to health?

In the past decade, the G8 played an important part in
the establishment or support of global health initiatives
that are at risk today of becoming part of the problem
rather than the solution for granting health coverage
to disadvantaged populations. The fragmentation
of financing for global health and increased transaction
costs contrast with the need for efficient and effective
health systems, and underline the need for a review of
quick-fix and selective approaches. In view of the pre-
csent economic crisis, a heightened commitment from
wealthy countries to sustain global health will be needed.

As chair of the G8 Summit 2009, Italy will have a unique
opportunity to renew its commitment to global health
and orient action towards a more effective approach.

Italy’s Official Development Assistance continues to
suffer from structural weaknesses, characterised by an
absence of clear political direction, weak management,
and inadequate and unstable funding.1 The health
sector has been no exception. Nevertheless, two aspects
deserve to be noted. First, as the result of contributions
to the Global Fund to Fight AIDS, Tuberculosis and Malaria,
launched at the Genoa G8 Summit in 2001, the
donations of Italian Official Development Assistance
for Health tripled between 2001 and 20072 (Italy is the
fourth largest contributor to the Global Fund along
with Japan, after France, the USA, and the UK).3 Italy
also engaged in new financing mechanisms, including
the International Financial Facility for Immunisation
and the Advance Market Commitment for vaccines
initiatives, by pledging substantial funds. Arguably,
this shift towards vertical initiatives has not been
accompanied by attempts to address concerns about
potential consequences for global health governance
and the negative system-wide effects at a country level.
The shift also contrasts with the longstanding guiding
principles of the Italian Development Cooperation in the
health sector—characterised by a comprehensive rather
than a selective approach to health—and also with
the domestic experience of the Italian National Health
Service that provides universal and comprehensive care.

Second, Italy’s contribution to global health
already goes beyond traditional Official Development
Assistance. The Italian National Health Service and the
decentralised public institutions (regions and munici-
palities) are increasingly engaged in development
cooperation. Civil society is very active (in Italy,
1433 not-for-profit organisations are associated with
international cooperation and solidarity activities,