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EDITORIAL

Decisions in HCT and wine-making

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It may not seem obvious at first but wine makers and haematopoietic cell transplanters (HCT) have a lot in common. Both spend a lot of time making decisions and the result of their decision making may not become apparent for a substantial amount of time later Fig. 1.

The first decision for HCT physicians is who to transplant. In the early days (1980s) it was easy. All adult patients with Acute Myeloid Leukaemia (AML) who were in remission following chemotherapy and who were under the age of 60 years, were offered an allogeneic HCT if they had an HLA compatible sibling. Similarly, adult patients with Acute Lymphoblastic Leukaemia (ALL) in first or subsequent remission and patients under the age of 30 years with Severe Aplastic Anaemia who had an HLA compatible sibling, were offered HCT.

There were other sundry conditions such as Multiple Myeloma (MM), Myelodysplasia (MDS) and some types of non-Hodgkin Lymphoma (NHL) in which HCT was offered in some centres. The situation is now more nuanced in AML, when molecular diagnoses help to determine which patients are likely to be cured with chemotherapy, and which patients should proceed to HCT [1–3]. However not all haematologists believe that the measurement of MRD (measurable residual disease) has been adequately standardised [4]. In adult patients with ALL in first or subsequent remission, opinion is divided as to the most appropriate treatment.

The role of unrelated HCT has dramatically altered with more precise HLA typing and the optimal use of Umbilical Cord blood (UBC) while haplo-identical transplants are evolving. The most difficult decision I had to make, in the 1980s, was to offer patients with Chronic Myeloid Leukaemia (CML) HCT knowing that they could be cured of their CML, but could succumb to transplant complications. While treatment with busulfan or interferon α could relieve their symptoms hope of a cure could not be offered. The advent of Tyrosine Kinase Inhibitors (TKIs) in the early 2000s, of course, significantly reduced the number of patients being referred for HCT.

HCT for MDS is a hotly disputed area [5, 6]. Patients with early MDS can undoubtedly be cured with HCT, albeit with a mortality rate of about 20%, whereas with careful medical management they may live for many years. The prognosis for advanced MDS remains poor even when fully matched HCT is undertaken. So, the decision when to offer HCT to a patient with MDS remains problematical.

The use of newer therapies such as monoclonal antibodies (moAbs), antibody-chemotherapy conjugates and genetically engineered T Cells (CAR-T Cells) offer new strategies and decisions as to when, and how, to use these modalities continues to evolve.

Decisions about the role of prophylaxis/treatment of suspected fungal and viral infections takes up many hours of the HCT physician's time. At the time of writing the role, if any, of COVID-19 in HCT remains unclear. So, many decisions that haematologists make about recommending HCT to patients are not clear cut.

Do wine makers have to make many decisions? Yes, they do. According to wine writer Hugh Johnson [7], (in my view one of the best wine writers in the English language), wine making requires many decisions. For example, whether to use mechanical or hand harvesting depends, to a certain extent, on the size of the vineyard [8]. Whether to remove the stems before crushing, is an important decision. Many winemakers remove the stems from red grapes but not from white. Stems contain tannins and may make a wine more astringent. As we know the basis of wine making is the conversion of sugar to alcohol by the action of yeasts. A lot of wine makers rely upon yeasts which naturally inhabit the grape skins (e.g., *Saccharomyces cervisiae*); others decide to use specially cloned yeasts or may add these to assist in alcoholic fermentation.

Malolactic fermentation or more correctly malolactic conversion is the conversion of bitter malic acid to

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Fig. 1 The villa at Petroio. The author and Dr Gianluigi Lenzi, neurologist and winemaker in Tuscany (Petroio near Siena) discussing wine-making decisions.

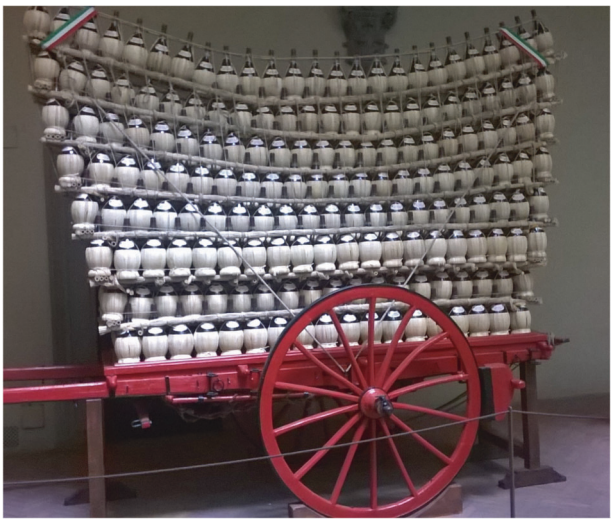

Fig. 2 Fiaschi. Popular in my student days but out of fashion today. Bottles, from Chianti, had a wicker partial covering. When empty a long red candle was inserted into the neck and lit. They adorned many student apartments and restaurants. The wine was awful.

lactic acid: $COOH-CHOH-CH_2-COOH$ converted to $COOH-CHOH-CH_3+CO_2$ by lactobaccilus (LAB). These bacteria occur naturally in grapes, usually *Oenococcus oeni*. It is common in red wines and some white wines, depending on the grapes (chardonnay is particularly susceptible to malolactic conversion).

Another major decision is the type of fermentation tank to use: wood, old or new oak, American or French, or Slavonian barrels, steel, clay amphorae, concrete or glass fibre. Further decisions involve the bottle type [Fig. 2], labels and last but not least, price.

So, like haematologists engaged in HCT wine makers have to make many decisions. Also, like haematologists, wine makers might not be able to assess the quality of their wine for some time after making it. Haematologists look for short-term toxicity and long-term side effects such as disease relapse or second malignancies.

So, when you are pressing that glass of wine to your lips take a moment to think of all the decisions which went into its making.

Compliance with ethical standards

Conflict of interest The author declares that he has no conflict of interests.

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