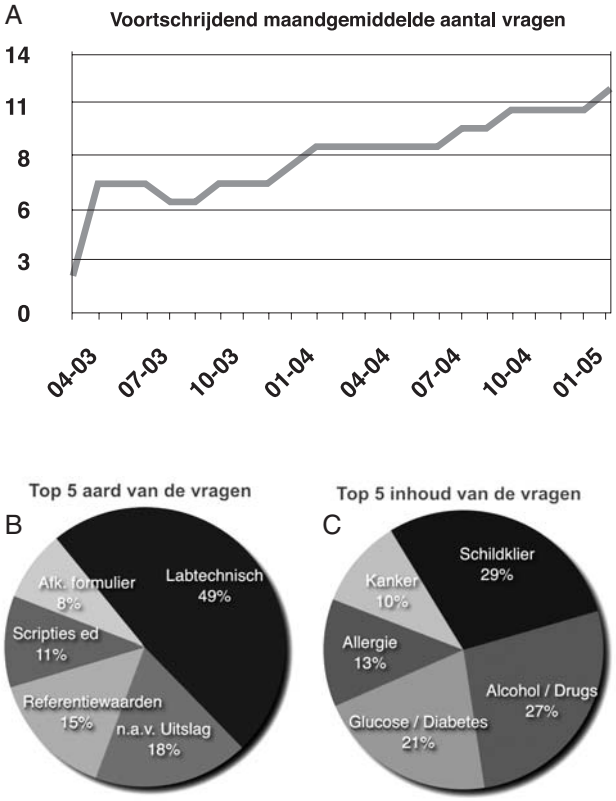
stukken maken ook (nog) deel uit van de top 5. Rekenen we deze categorie niet mee, dan komen vragen over medische terminologie en ziektebeelden als vijfde in beeld. In veel mindere mate dan aanvankelijk werd verwacht, stellen mensen vragen van zuiver klinische aard (4%). Deze vragenstellers werden alle rechtstreeks verwezen naar een (huis)arts of specialist. In een aantal andere gevallen (4%) werd hetzelfde advies gegeven. Andere bronnen waar naar verwezen werd zijn met name het Diagnostisch Kompas, medischlab.nl en de websites op de linkpagina (totaal 18%).
Kijken we naar de onderwerpen waarover de meeste vragen komen, dan zijn schildklier, alcohol/drugs en diabetes het meest prominent aanwezig, allergie en kanker in iets mindere mate. Trombose, bloedgroep, SOA en DNA worden naar verhouding minder genoemd.
Naar aanleiding van het grote aantal vragen over alcohol en CDT is een uitgebreide FAQ opgenomen. Ook is inmiddels een lijst met toelichting op de meest aangehaalde afkortingen van het aanvraagformulier geplaatst.

Conclusie
De faciliteit voorziet in een behoefte. Indien meer publiciteit wordt gezocht, zal het aantal vragen waarschijnlijk verder toenemen. Onbekend is echter hoeveel vragen reeds worden 'afgevangen' door de rubriek veelgestelde vragen. Als men bedenkt dat het onderdeel Publieksinformatie dagelijks gemiddeld meer dan 100 bezoekers telt, zou dit wel eens aanzienlijk kunnen zijn. Het aantal FAQ's, zeker als er veel vraag naar een bepaald onderwerp is, zoals met name over schildklier-, glucose- en allergieonderzoek, zou verder kunnen worden uitgebreid. Het aansluiten van de antwoorden bij het niveau van de vragensteller blijft een zaak van voortdurende aandacht.



Figuur 1. Aantal vragen per maand en top 5 van de aard en de inhoud van de vragen.

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Mutation of *FLT3* is not a general phenomenon in CD117-positive T-ALL

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Introduction
CD117 is considered to be a marker of leukemic cells committed to the myeloid lineage, however up to 11% of T-ALLs have been found to express CD117 (1). Activating mutations in the *FLT3* gene are common in acute myeloid leukemia (AML) but are rarely found in acute lymphoblastic leukemia (ALL) (2). Recently, a subset (3 out of 55) of adult T-ALLs characterized by expression of CD117 (in >90% of T-lymphoblasts) and *FLT3* mutations (either internal tandem duplications (ITD) in the juxtamembrane region or mutations in the activation-loop coding region) was described (3). These data suggested that CD117 expression in T-ALL lymphoblasts might identify a subset of T-ALLs in which activating *FLT3* mutations are essential in oncogenesis. If *FLT3* mutations would be present in all CD117-positive T-ALLs, up to 11% of all T-ALL patients could potentially benefit from therapy with FLT3 inhibitors, which are currently under investigation for AML treatment (2, 4).

Results
We report here on the *FLT3* mutation status of a 75 year old man diagnosed with CD117-positive T-ALL. The patient presented with pancytopenia and anemia.

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Bone marrow analysis revealed 70% blasts with an L1 ALL morphology according to the French-American-British classification. There was no cytochemical evidence of myeloid differentiation, i.e. Sudan black B, specific and non-specific esterase stains were negative. Flowcytometry demonstrated 85% blasts, 9% T-lymphocytes, 1% B-lymphocytes, 2% granulocytes, and <1% monocytes. The blasts were classified as T-lymphoblasts based on intracytoplasmic CD3 expression (Figure 1). Furthermore, >90% of the blast cells were positive for CD117, CD2, CD7, CD13, CD45, and CD56, whereas CD34, CD33, CD5, and CD19 were expressed on a subset of blast cells only (about 75%, 30%, 30% and 40% of blasts, respectively). Blast cells did not significantly express TdT, MPO, CD1a, CD4, CD8, CD10, CD14, CD15, CD22, CD65, CD133 and SmCD3 (all <10% positive). Of importance, CD135 (FLT3) expression was weak/negative on the T-lymphoblasts (Figure 1).
Cytogenetics revealed a complex karytoype in 73% of metaphases: 46, XY, der(1)t(1;9)(p34;q34)t(1;3)(q22;q22), der(3)t(1;3), del(5)(q21q34), der(9)t(1;9), t(12;17)(q24;q2?1). The balanced translocation between chromosomes 1 and 9 might involve the *ABL* gene on 9q34. The other translocations have been observed in MDS/AML, like the del(5), or in rare cases of CML, like the t(1;3), t(1;9) and t(12;17), but have never been described in combination so far.
RT-PCR analysis showed no ITD in the *FLT3* juxtamembrane region (Exon 14 and 15) (5). Furthermore, sequence analysis of the *FLT3* activation-loop coding region (exon 20) showed the absence of currently-known activating mutations (D835, I836, 840GS, N841 and Y842C) (6).

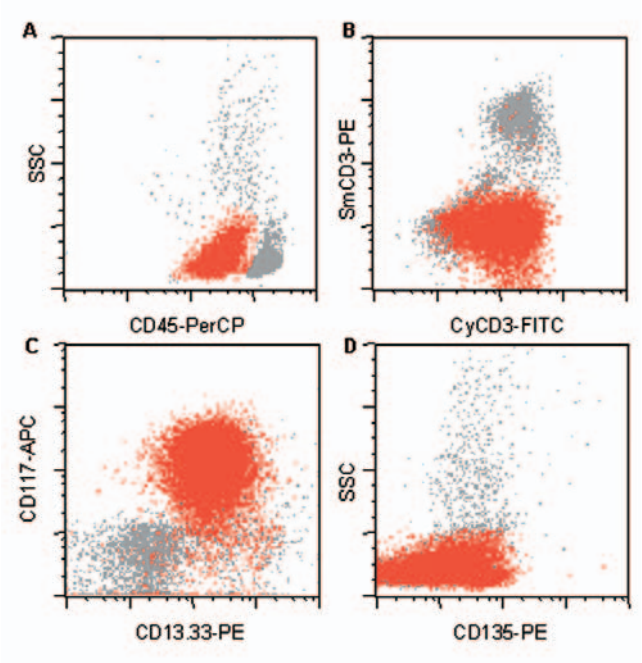

Figure 1. Immunophenotype of the T-lymphoblasts. Immunophenotyping was performed using four-color labelings and data were acquired on a FACS Calibur (BD Biosciences, San Diego, CA). (A) The T-lymphoblasts (85% of the leukocytes) showed a low side scatter and intermediate expression of CD45, which clearly distinguished them from the remaining normal lymphocytes (10%), monocytes (<1%), and granulocytes (2%). By gating on the SSC-CD45 characteristics, the immunophenotype of the T-lymphoblasts was further evaluated, showing intracytoplasmic CD3 expression in the absence of surface membrane CD3 expression (B), positivity for CD117 and CD13/CD33 (C), and no/weak expression of CD135 (D).

Conclusion

Immunophenotypically the case presented here is an immature T-ALL expressing CD117 and CD13, comparable to the three cases described earlier (3). However, the remaining immunophenotype of our patient showed some differences, with (partial) positivity for CD56, CD33 and CD5, and negativity for TdT. More important, our patient lacked significant CD135 expression and showed no activating *FLT3* mutations. Although we cannot exclude the presence of mutations outside exon 14, 15 and 20, our data strongly suggest that CD117-positive T-ALLs do not necessarily carry *FLT3* mutations. Apparently, CD117-positive T-ALL are more heterogeneous than previously reported (3). Further research into the frequency of *FLT3* mutations in CD117-positive T-ALL is necessary to establish the correlation between the immunophenotype of T-lymphoblasts and *FLT3* mutations. Such analysis will finally show which percentage of patients with CD117-positive T-ALLs might benefit from therapy with FLT3 inhibitors.

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