

# Understanding off-label use and the information needs of patients: a pilot Eurordis survey in rare diseases



## Drug Information Transparency and Access (DITA) Task Force

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# Background

- 4000 to 6000 distinct rare diseases
  - Defined as  $<1/2000$  or  $<250,000$  patients EU-wide
  - 4-6% of EU population affected
- More than 1000 OMP designated
  - Of which 71 are authorised for 83 rare indications
- Most patients with a rare disease are not treated with an authorised orphan medicine
  - when they are treated
- Off-label use is the rule, not the exception in RD
- 18% of patients with a RD rejected by HCP
  - 85% due to disease complexity (EurordisCare 3 survey)



# One example



- Jenny's parents' garage
- In infancy, J was diagnosed with cystinosis
- Medically, she suffered renal failure by the age of 6 (+ hypothyroidism, insulin-dep. diabetes, hepato-splenomegaly with hypertension, muscle and cerebral involvement, photophobia)
- Her parents refused to sit idly by
- They contacted pharma companies
- They learned how to treat their child “off-label”, where nobody had been before
- Getting information directly from the company was life-saving
- Jenny received daily dialysis until age 22
- Her parents created Climb, the National Information Centre on Metabolic Diseases in the UK, so children like Jenny can live longer



# Objectives

**Document patients' experience with OL use**

**Learn about the information patients receive**

**Create database of off-label uses in rare diseases**

**Explore how patients handle ADRs with OL use**

**Define future actions on OL use in rare diseases**

OL: Off-label

ADRs: Adverse Drug Reactions



# 90 conditions, 105+ off label uses

Condition	Product	Indication	Off label use
Dravet syndrome	Urbanyl	Epilepsy, but not recommended for use in children between the ages of six months and three years	5 mg twice a day since the age of 6 months. With micropakine, diacomit, epitomax
Friedreich Ataxia	Idebenone	Alzheimer's disease and other cognitive defects	720 mg/day for 12 years
Behcet disease	Thalidomide	Multiple myeloma	1 mg/kg/week to 1 mg/kg/day

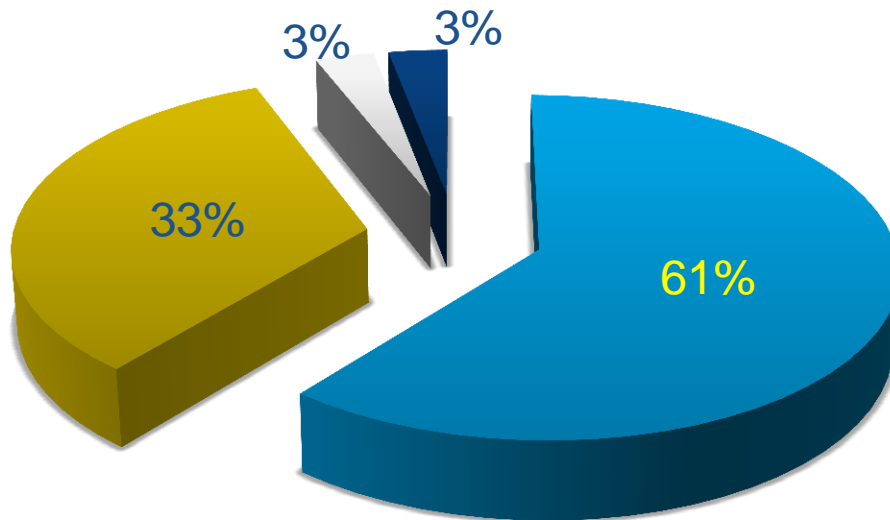


# Methodology

- Online survey, 5 languages
- Short description on what is off-label, why we were doing the survey with (18) questions
- Open for 2 months (Eng) or 1 month (other languages), May-Jul 2012
  - One reminder sent in all languages, two in Spanish
- Developed by DITA at Eurordis from Nov 2010
- Target population – people with rare diseases who had used drugs off-label in the past



# Who answered our survey?

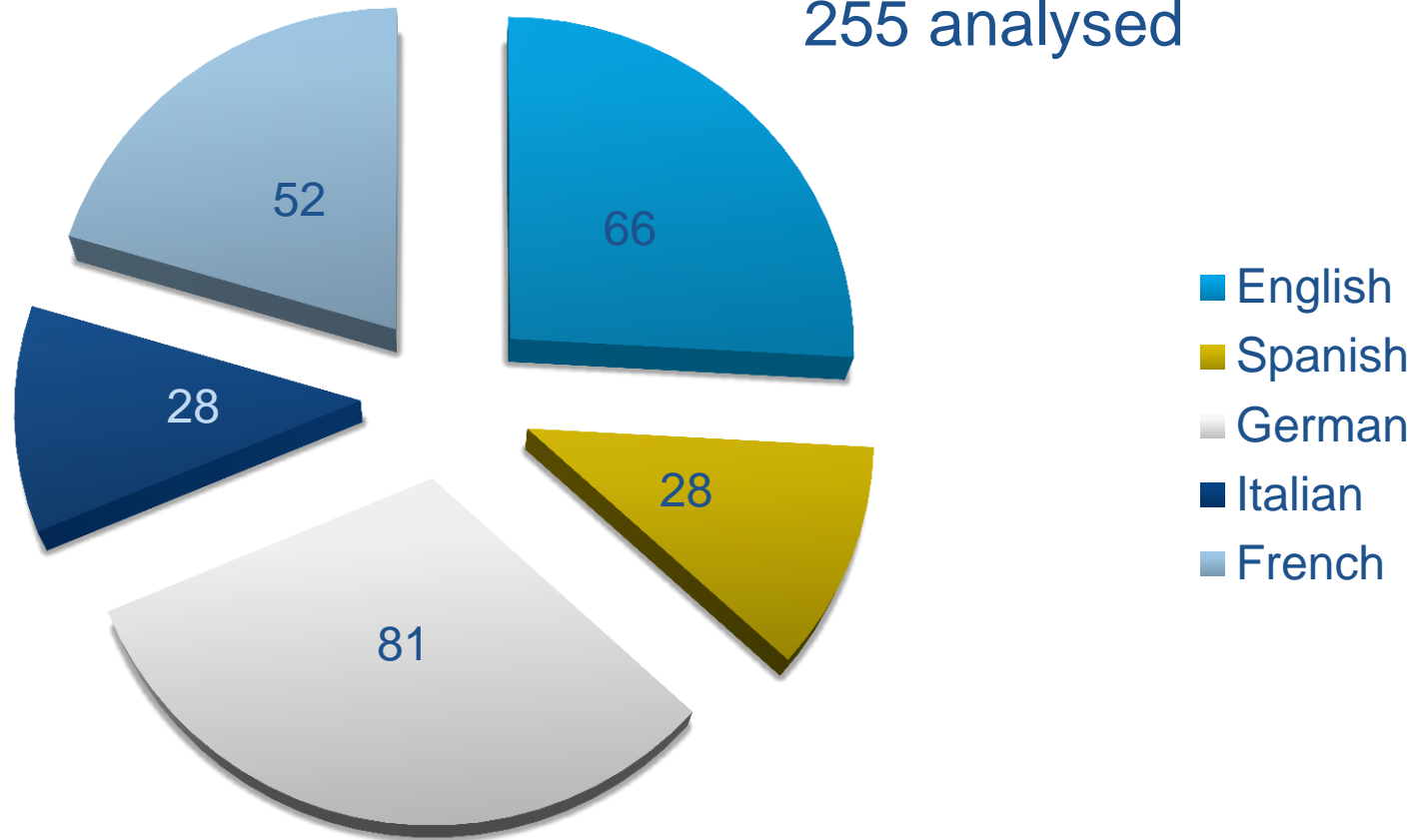


- The person taking the treatment
- A parent
- Another family member
- Another care provider



# Respondents' language

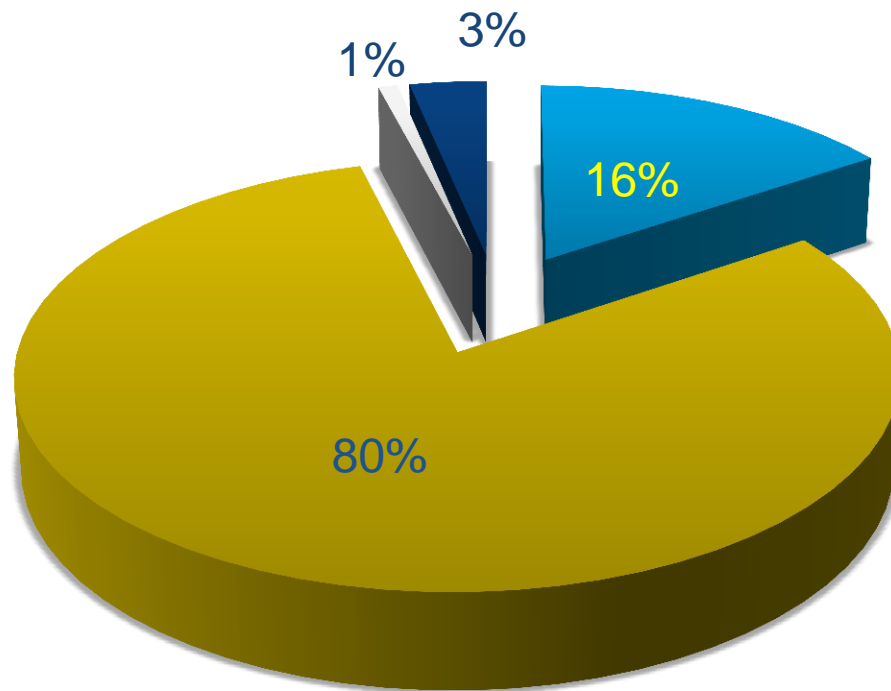
294 responses received  
255 analysed







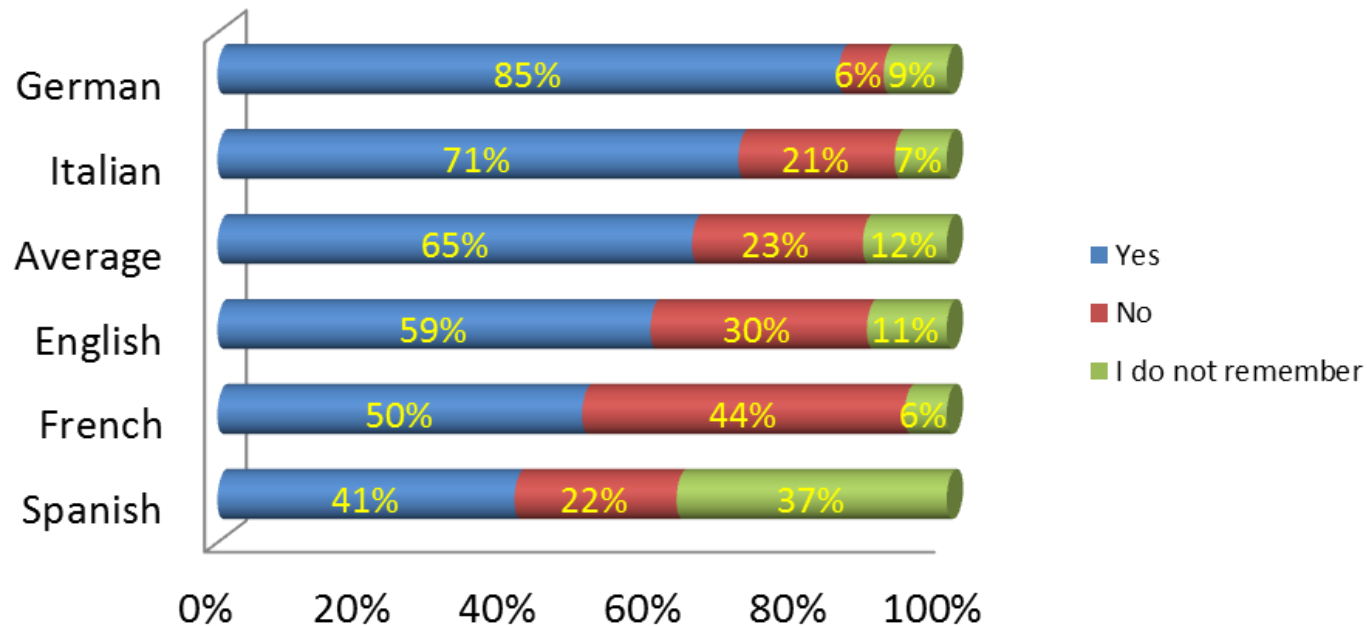
# Who proposed the (OL) use?



- I did
- The doctor
- I don't remember
- Another professional



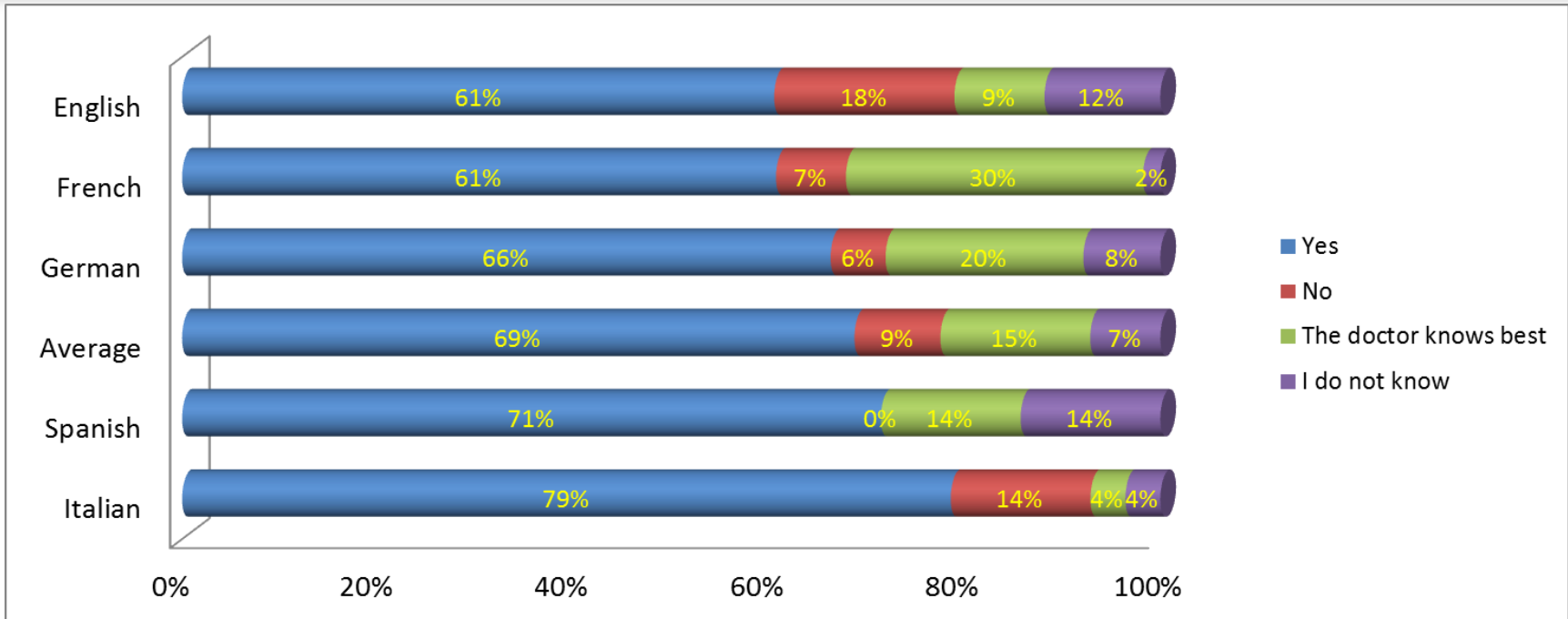
# Was it explicitly discussed that the drug was off-label?



	Yes	No	I do not remember
German	69	5	7
Italian	20	6	2
English	38	19	7
French	26	23	3
Spanish	11	6	10
TOTAL	164	59	29



# Should there be more explanation about risk/benefit?



	Yes	No	The doctor knows best	I do not know
French	34	4	17	1
English	46	14	7	9
German	59	5	18	7
Spanish	20	0	4	4
Italian	22	4	1	1
<b>TOTAL</b>	<b>211</b>	<b>27</b>	<b>47</b>	<b>22</b>

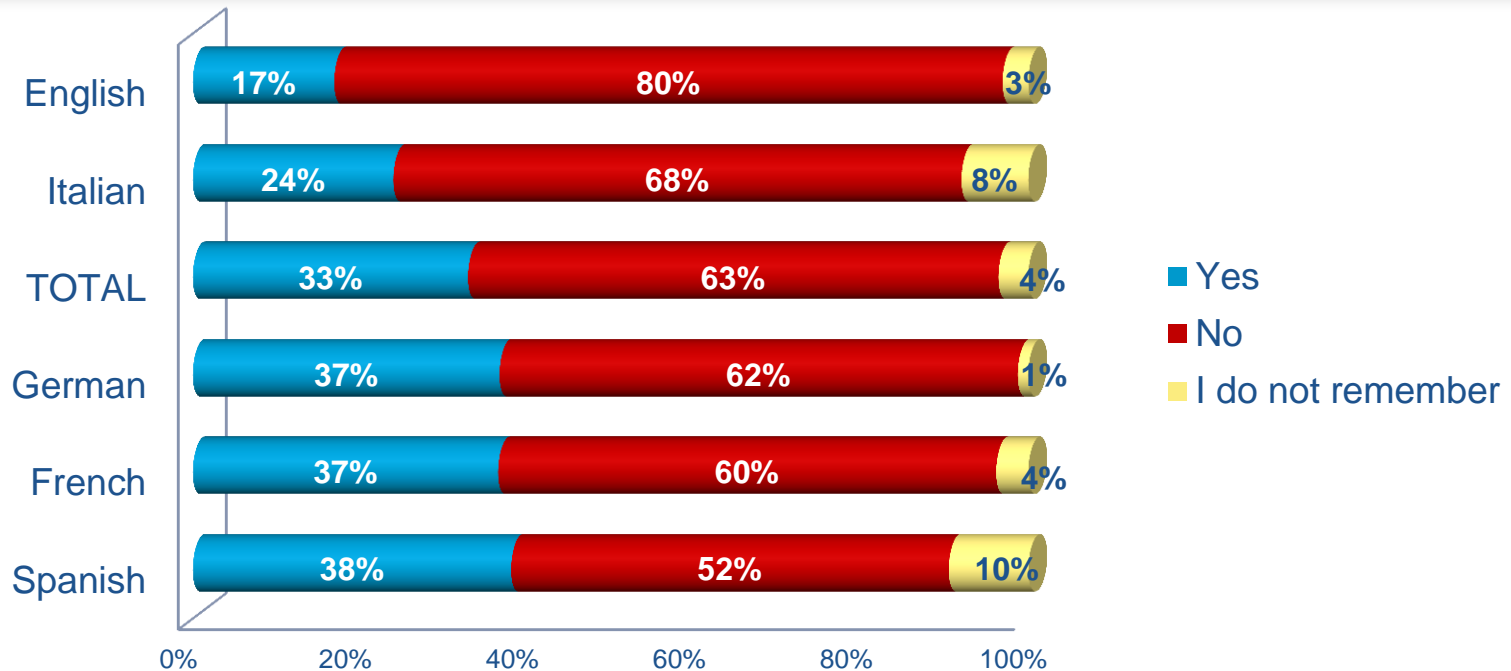


# Common “more explanation” comments

- ...the side effects are what patients should be told about, and how severe (they may be)
- We did not know it was an off-label indication until my father went blind due to the drug
- Helpful – a phone line, email link, Internet research, signed written consents
- The doctor was very clear, I understood it all...
- I find myself desperately accepting whatever the doctor offers...
- Doctors do not know everything



# Were there adverse events while taking the drug?



	Yes	No	I do not remember
English	11	52	2
Italian	6	17	2
German	29	49	1
French	19	31	2
Spanish	8	11	2
<b>TOTAL</b>	<b>83</b>	<b>160</b>	<b>9</b>

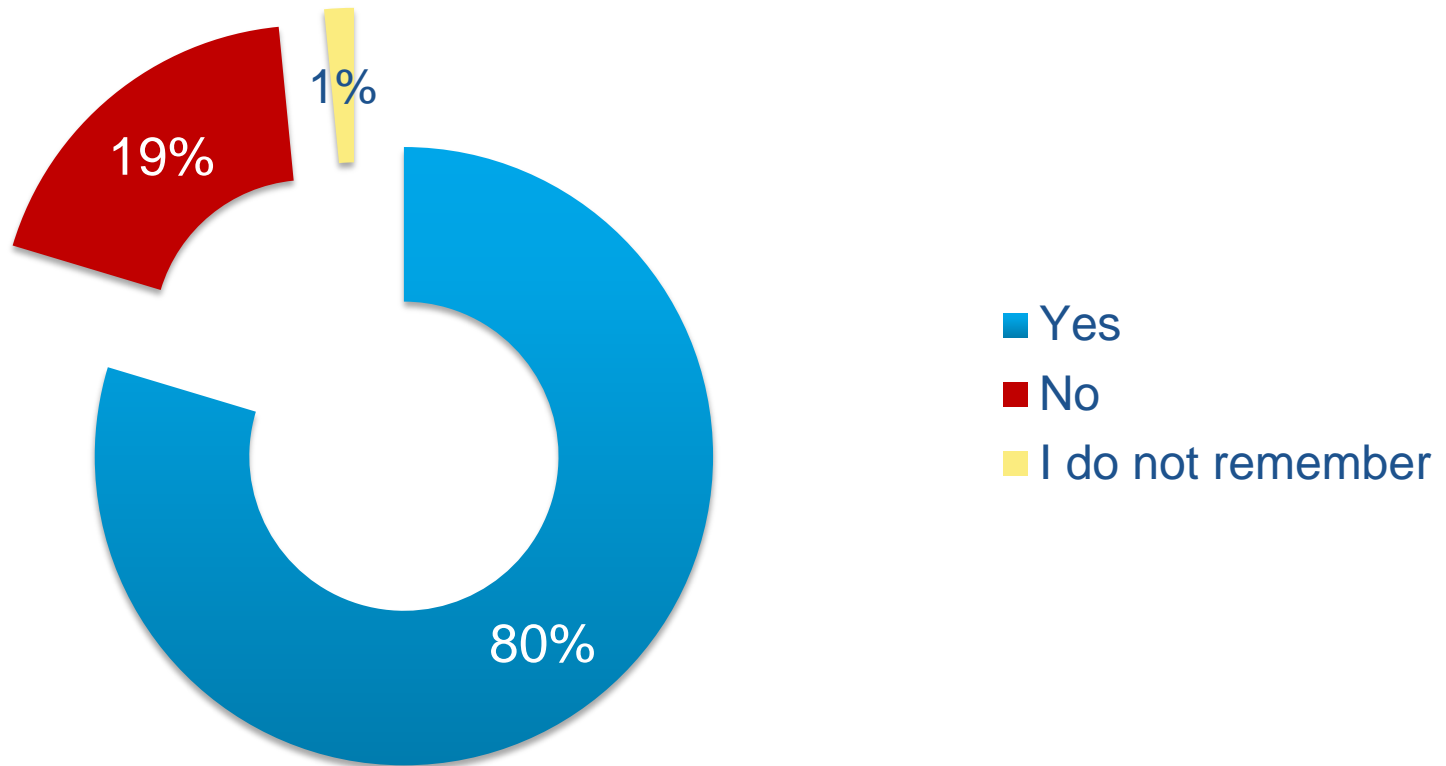


# Adverse events descriptions

- ...it did incapacitate my abilities of clear and rapid thinking permanently, it produces a mental blockage and intracranial pressure. It also caused constipation and/or diarrhoea.
- (there has been a drop) in my blood platelets, haemoglobin and red cells. I have required various transfusions of platelets and red corpuscles
- the copper ... gets deposited in the brain, he was temporarily incapacitated, ... was hospitalised and now has some sequelae
- Severe aches, itching, headaches, dizziness and hyper-sex drive which continued for approx 5 years - never investigated by a health professional or even warned (about them)...
- Tunnel vision, lack of coordination, frequent falling, impaired brain function, blackouts. While driving home from work, I blacked out in the car for several seconds.
- Nerve end damage to my fingers and feet. Pins and needles in my feet and hands. I was violently ill, throwing up, fever, rash - no permanent damage

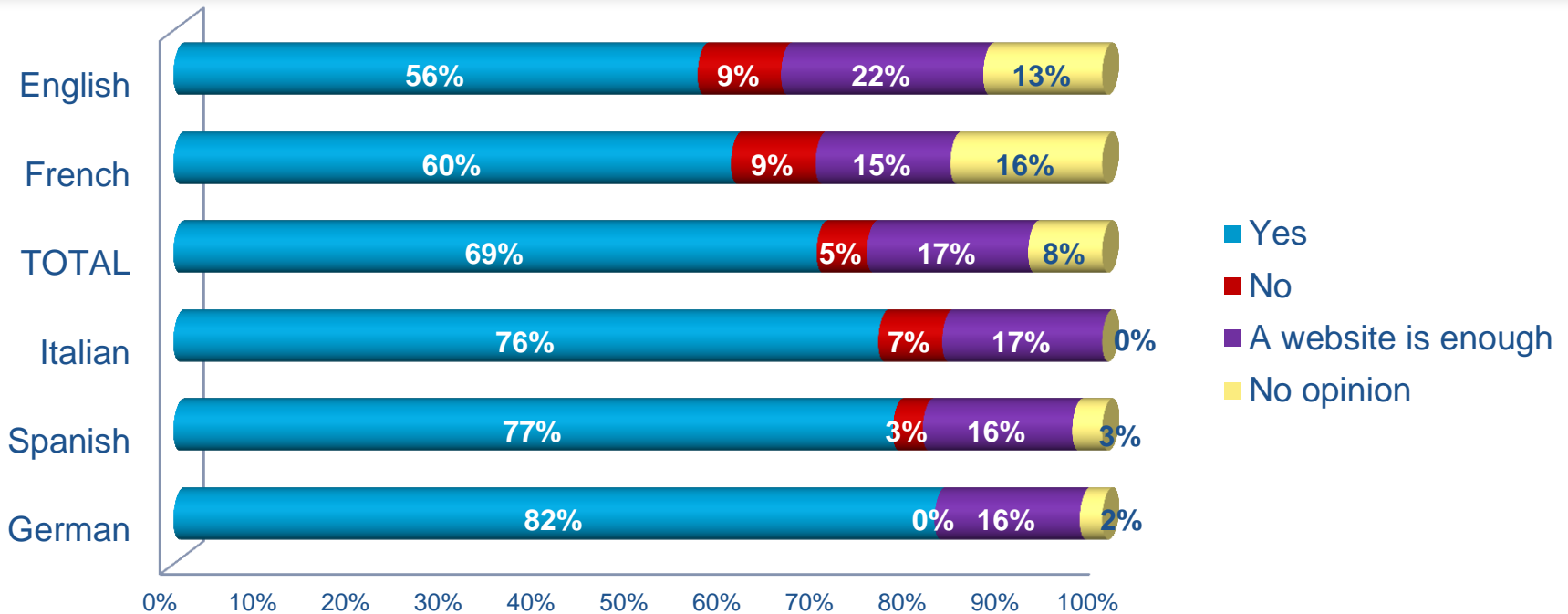


# Did you report the adverse event?





# Should there be a dedicated help line to report side effects?

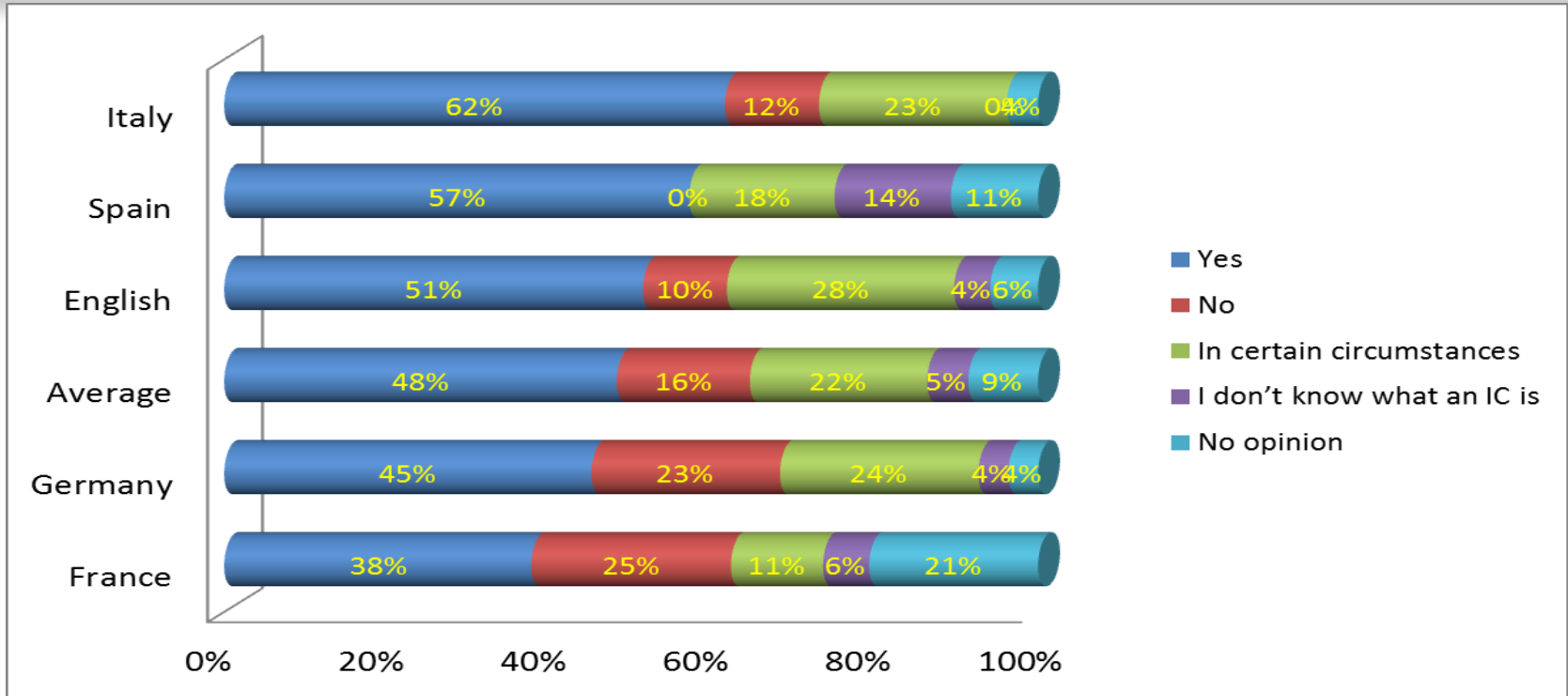


	Yes	No	A website is enough	No opinion
English	44	7	17	10
French	33	5	8	9
Italian	22	2	5	0
Spanish	24	1	5	1
German	68	0	13	2
<b>TOTAL</b>	<b>191</b>	<b>15</b>	<b>48</b>	<b>22</b>





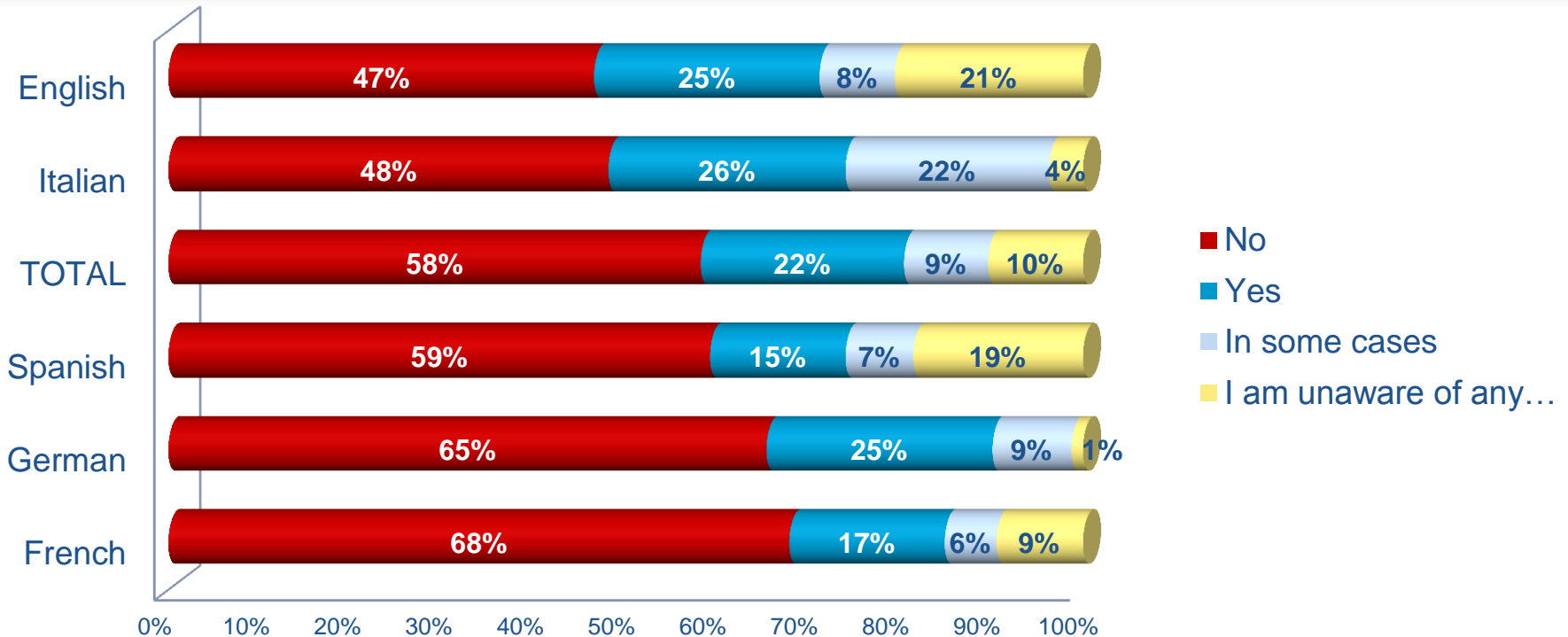
# Should an informed consent form be required for off-label?



	Yes	No	In certain circumstances	I don't know what an IC is	No opinion
Italian	16	3	6	0	1
Spanish	16	0	5	4	3
English	35	7	19	3	4
German	37	19	20	3	3
French	20	13	6	3	11
<b>TOTAL</b>	<b>124</b>	<b>42</b>	<b>56</b>	<b>13</b>	<b>22</b>



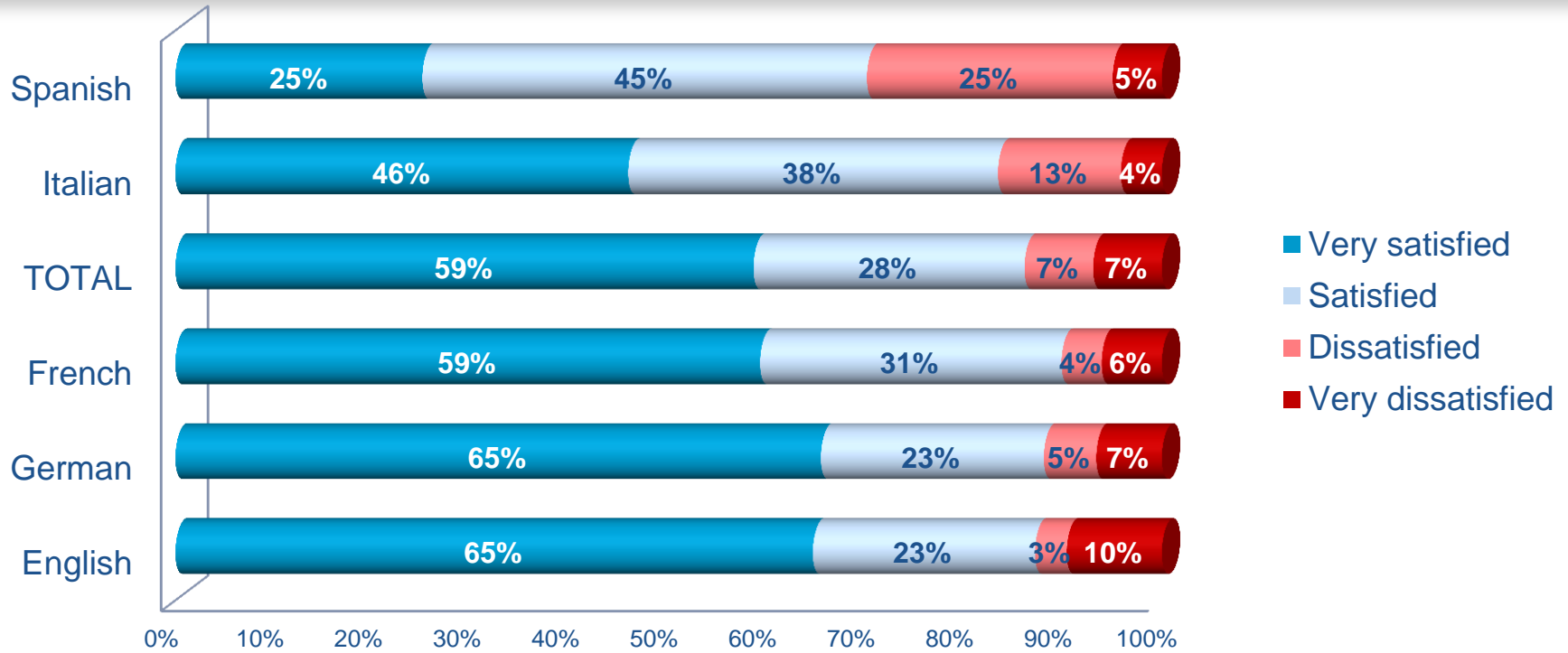
# Were there any supply or reimbursement issues?



	Yes	In some cases	No	I am unaware of any...
English	18	6	34	15
Italian	7	6	13	1
Spanish	4	2	16	5
German	20	7	53	1
French	9	3	36	5
<b>TOTAL</b>	<b>58</b>	<b>24</b>	<b>152</b>	<b>27</b>



# Your rating of the off-label experience



	Very satisfied	Satisfied	Dissatisfied	Very dissatisfied
English	40	14	2	6
Spanish	5	9	5	1
German	49	17	4	5
Italian	11	9	3	1
French	29	15	2	3
<b>TOTAL</b>	<b>134</b>	<b>63</b>	<b>16</b>	<b>16</b>



# Your OL experience

- There aren't many specific treatments and there is not a lot of research because it isn't money-making for the big pharma companies, (so) other drugs do help alleviate some of the symptoms, although they are not indicated, and as long as they explain about the risk/benefit, it (*the OL*) seems fine to me
- It (*the treatment*) seems to be working
- The treatment has given me 18 months remission and I have not had to take any other medication since my treatment
- I do think that records should be kept of off-label usage so they can be collated to inform both medics and patients of the success or otherwise of the drug ...
- Depends on the drug – some are failures, others work well
- No significant changes, the condition is not getting worse
- It worked but there are lots of side effects



# Discussion

- Patients' and doctors' ability to communicate fully is limited
  - OL risks can be ameliorated by fuller communication at all steps in the therapeutic process
- Patients' understanding of OL is limited
- Types of adverse events here are significant – even when only 1/3 experience them, those who do have stories to tell
- The less information/understanding of OL, the less comfortable with OL & their treatment a person may be
  - Does this also coordinate with comfort of being able to share with your doctor?
- Patients need and want more (and better) treatments
- Patients need and want more information
  - How can this be done?



# Off-label

- Back up slides

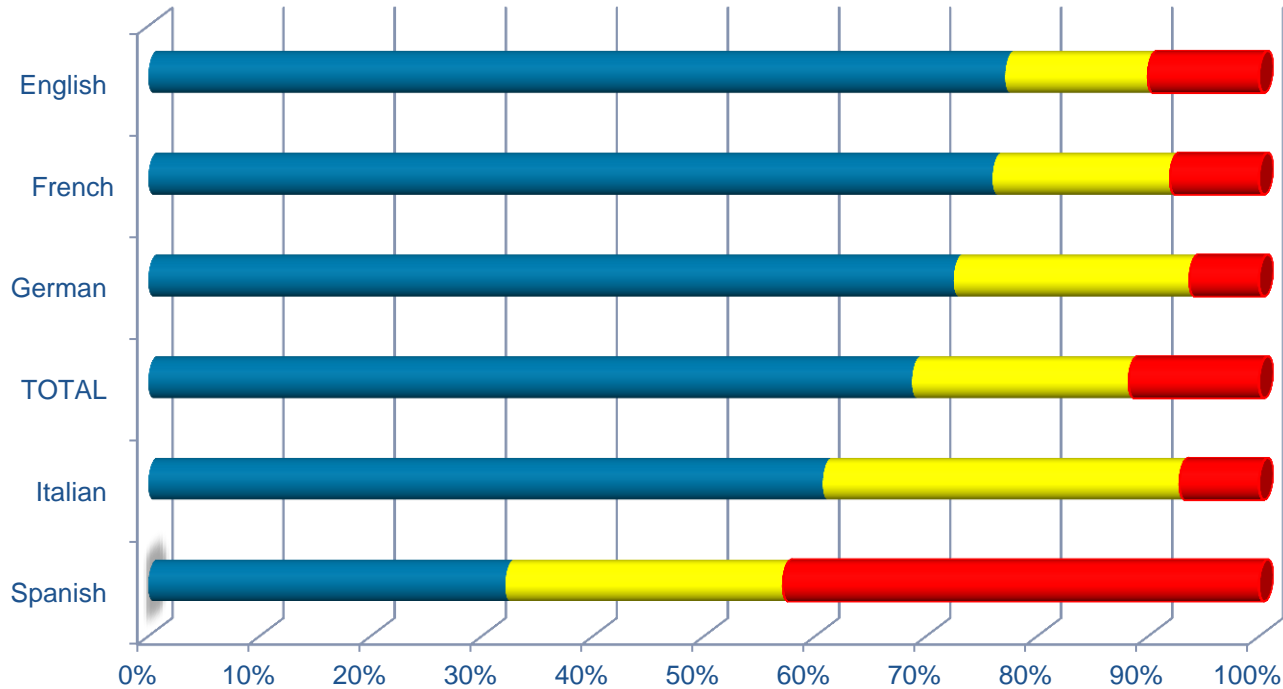


# 90 conditions, 105+ off-label uses

Condition	Product	Indication	Off label use
Sotos syndrome + congenital heart disease + heart failure as a baby	IV furosemide	congestive heart failure and edema	As a baby used IV furosemide orally to reduce fluid load as there was no suitable per os dose
Macular degeneration	Avastin	Renal Cell carcinoma, Non-Small-Cell Lung carc., Breast, Colorectal and Ovarian neoplasms	My father had an injection of Avastin for macular degeneration on 20/02/2012 and the drug was contaminated. He went blind within two hours. I now know 14 patients who were affected by this batch
Narcolepsia cataplexia	teronac	Short-term (i.e., a few weeks) treatment of exogenous obesity (amphetamine like)	1 dose per day, lifelong, with Modiodal and Effexor

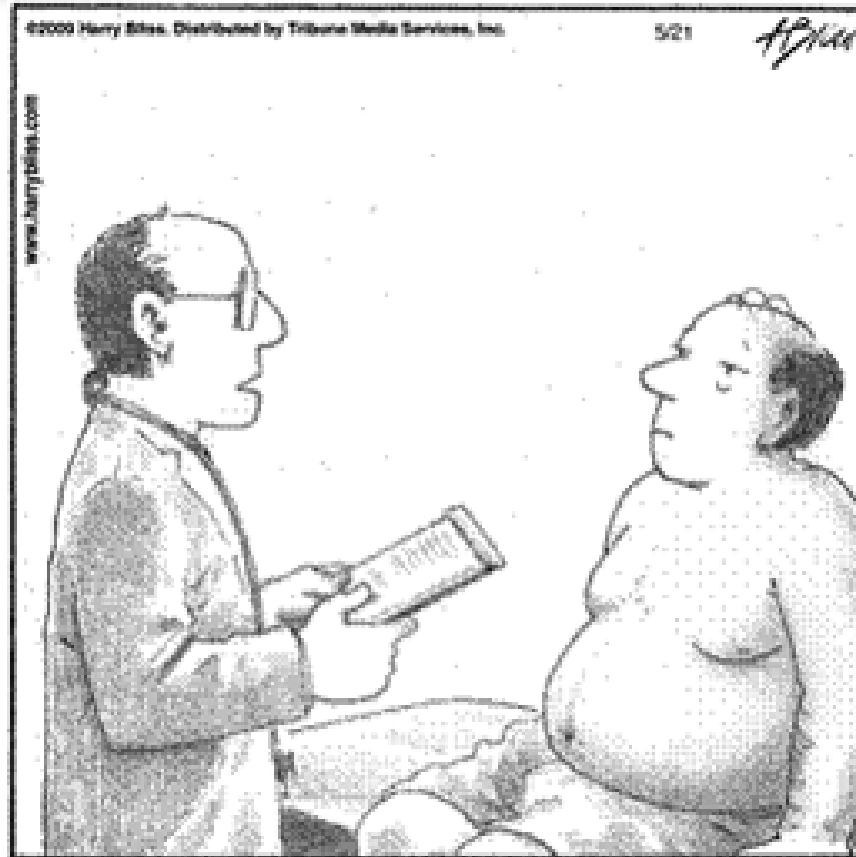


# Were you comfortable with it being off-label?



	Yes	Somewhat	No
English	54	9	7
French	38	8	4
German	58	17	5
Italian	17	9	2
Spanish	9	7	12
<b>TOTAL</b>	<b>176</b>	<b>50</b>	<b>30</b>





**"Well, yes, I suppose I could explain the test results in 'plain English' — but then you'd know how sick you are."**