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# Targeted therapy in patients with PIK3CA-related overgrowth syndrome

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**Supplementary Table 1:** Demographic characteristics. In this Supplementary Table, we provide the principal demographic characteristics of the patients, the clinical manifestation and the *PIK3CA* mutation.

Patient	Sex	Age (yrs)	Ethnicity	Clinical manifestation and reason of BYL719 introduction	<i>PIK3CA</i> mutation		Tissue	Mosaicism	BYL719 Dosage (mg/d)
					cDNA change	AA change			
1	F	4	Caucasian	-Upper right limb overgrowth with intrathoracic tumor -Extreme tiredness -Sleep disturbance -Life threatening complication -Dyspnea NYHA III	c.1633G>A	p.Glu545Lys	Skin	3.0%	50
2	F	4	Caucasian	-Left lower limb overgrowth -Amputation envisaged	c.3140A>G	p.His1047Arg	Skin	25.8%	50
3	F	5	Caucasian	-CLOVES -Chronic gastrointestinal bleeding	c.1638G>C	p.Gln546His	Skin	6.0%	50
4	F	5	Caucasian	-Left hemifacial hyperplasia -Growing of the lesion despite multiple surgery	c.3140A>G	p.His1047Arg	Lipoma	23.0%	50
5	M	7	Caucasian	-CLOVES	c.1258T>C	p.Cys420Arg	Skin	10.4%	50
6	F	10	Caucasian	-CLOVES -Scoliosis surgery scheduled	c.1624G>A	p.Glu542Lys	Skin	50.0%	50
7	M	11	North African	-CLOVES -Chronic gastrointestinal bleeding -Heparin treatment -Dyspnea NYHA III	c.1258T>C	p.Cys420Arg	Skin	33.0%	50
8	F	11	Caucasian	-CLOVES -Dyspnea NYHA III	c.3127A>G	p.Met1043Val	Skin	12.4%	50
9	F	13	North African	-CLOVES -Left leg amputation -Vascular tumor infiltrating the right kidney -Voluminous splenomegaly -Chronic gastrointestinal bleeding -Heparin treatment	c.3140A>G	p.His1047Leu	Skin	33.0%	50

				-Dyspnea NYHA III					
<b>10</b>	M	14	African	-Bilateral overgrowth of lower limbs -Dyspnea NYHA II -Asthenia	c.3132T>G	p.Asn1044Lys	Skin	6.6%	50
<b>11</b>	M	14	Caucasian	-Overgrowth of the right buttock -Intraabdominal vascular tumor infiltrating the left kidney and spinal nerve -Chronic hematuria -Pain with opioid dependency -Permanently confined to bed	c.1624G>A,	p.Glu542Lys	Skin	7.46%	50
<b>12</b>	M	15	Caribbean	-Multiple large tumors of the trunk and the back -Surgery envisaged	c.3140A>G	p.His1047Leu	Lipoma	17.4%	50
<b>13</b>	M	16	Caucasian	-MCAP -Left hemifacial hyperplasia	c.1624G>A	p.Glu542Lys	Tongue	16.0%	50
<b>14</b>	F	16	Caucasian	-MCAP -Noninfectious palpebral cellulitis steroid dependent	c.2176G>A	p.Glu726Lys	Skin	38.0%	50
<b>15</b>	M	19	North African	-Left foot overgrowth -Unstable and painful walking -Amputation envisaged	c.3140A>G	p.His1047Arg	Skin	14.0%	250
<b>16</b>	M	32	Caucasian	-Lower right limb overgrowth - Unstable and painful walking -Amputation envisaged	c.3140A>G	p.His1047Arg	Skin	19.0%	250
<b>17</b>	F	50	Caucasian	-Generalized hypertrophy -Severe and diffuse pain with opioid dependency -Permanently confined to bed -Dyspnea, NYHA III -Overweight	c.1133G>A	p.Cys378Tyr	Skin	5.0%	250

CLOVES: Congenital Lipomatous Overgrowth, Vascular malformations, and Epidermal nevi syndrome. MCAP: Megalencephaly-capillary malformation syndrome. F: female. M: Male. NYHA: New York Heart Association.

**Supplementary Table 2:** Response to treatment. In this Supplementary Table, we provide the clinical and radiological responses per patient at 3- and 6-months post BYL719 introduction.

Patient	Target lesion						Other clinical manifestations
	Clinic (measured circumference)	Clinic (% of change)		Radiology	Radiology (% of change)		
		3 months	6 months		3 months	6 months	
1	Right arm	-15.4	-19.2	Intrathoracic tumor	-42.1	-63.9	-Improvement of tiredness -Improvement of sleep -No more dyspnea
2	Buttock	-10	-16.7	Left buttock	-28	-49	-Improvement of tiredness
3	Left thigh	-12.8	-15.2	Left thigh	-22.2	-32.8	-Improvement of tiredness -No more bleeding
4	-	-	-	Tumor face volume	-35.8	-41.3	
5	Left thigh	-9.6	-11.6	Subcutaneous lipoma	-17.3	-34.8	-Improvement of tiredness
6	Tumor of the back	-12.8	-15.2	Tumor of the back	-22.2	-32.7	-Improvement of tiredness -Surgical corset removed
7	Left thigh	-17.2	-25.1	Left thigh	-11.1	-18.1	-Improvement of tiredness -No more bleeding -Heparin treatment stopped, no more DIC -No more dyspnea
8	Chest girth	-11.1	-13.3	Subcutaneous lipoma	-11.8	-18.7	-Improvement of tiredness
9	Right thigh	-15.9	-18.2	Right kidney tumor	-67.5	-73.1	-Improvement of tiredness -No more bleeding -Heparin treatment stopped, no more DIC -No more dyspnea -Volume reduction of the splenomegaly
10	Buttock	-13.2	-14.9	Right buttock	-20.3	-40.6	-Improvement of tiredness -No more dyspnea
11	Buttock	-7.6	-14.2	Left kidney tumor	-52.5	-68.8	-Improvement of tiredness -No more hematuria -No more pain, opioids stopped after 2 months -Capable to walk

							-Went back to school
<b>12</b>	Back tumor	-11.4	-14.8	Back tumor	-30.2	-37.2	-Improvement of tiredness
<b>13</b>	-	-	N/A	Tumor face volume	-22.1	-31.3	-Improvement of tiredness -Enhancement of the cognitive function and behavior
<b>14</b>	Waist circumference	-13.4	-16.6%	Waist circumference	-18.1	-22.1	-Improvement of tiredness -Enhancement of the cognitive function and behavior -Healing of the cellulitis, steroids stopped without flare
<b>15</b>	Left foot	-11.9	-14.8	Left foot	-17.2	-27.9	-Improvement of tiredness -Improvement of the walking distance
<b>16</b>	Right foot	-8.6	-13.8	Right foot	-30.2	-37.2	-Improvement of tiredness -Improvement of the walking distance
<b>17</b>	Waist circumference	-21.4	-24.5	Waist circumference	-17.6	-24.9	-Improvement of tiredness -No more dyspnea -No more pain, opioids stopped in 2 weeks -Capable to walk -Dramatic weight loss

DIC: Disseminated intravascular coagulation. -: Not appropriate for measurement.